

Rosario Rizzuto

Dept. Biomedical Sciences

University of Padua

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Personal data

Born in Rome (Italy) on April 15th, 1962

Living in Padua, Italy

Married, 3 children

Current position

Professor of General Pathology, University of Padua, Italy

President of the National Center on Gene Therapy and RNA-based therapies

Work experience

2021-date

Cassa di Risparmio di Padova e Rovigo

Member of the General Council

2019-2021

Coimbra Group Universities

Member of the Rectors' Advisory Group

2019-2021

European University Association (EUA)

Member of the Research Policy Working Group

2019-2021

Conference of the Rectors of Italian Universities (CRUI), Rome, Italy

Member of the steering committee ("Giunta") and delegate for Research and Innovation

Coordinator of the Research Committee

2015-2021

University of Padua, Padua, Italy

Rector

2009-2015

Department of Biomedical Sciences

University of Padua, Padua, Italy

Head of the Department

2008-date
Department of Biomedical Sciences
University of Padua, Padua, Italy
Full Professor of General Pathology

2007-2008
School of Pharmacy
University of Ferrara, Ferrara, Italy
Dean of the School

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

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

1992-1998
School of Medicine
University of Padua, Padua, Italy
Assistant Professor of General Pathology

1991-1992
Department of Experimental Biomedical Sciences
University of Padua, Padua, Italy
Research Associate

Education

1991
University of Padua, Padua, Italy
Department of Experimental Biomedical Sciences
Ph.D. in Molecular and Cellular Biology and Pathology

1987-88
Columbia University, New York, USA
H. Merritt Center for the Study of Neuromuscular Disorders
2-year research stage

1986
University of Padua, Padua, Italy
School of Medicine
Medical degree, summa cum laude

Honours, Awards and Memberships

2020: Commander of the order of merit of the Italian Republic

2014: Antonio Feltrinelli Award of the Accademia dei Lincei

2004: Theodore Bucher Medal

2002: Chiara D'Onofrio Prize

2001: Biotec Award

2017-date: Fellow of the *Istituto Veneto di Scienze, Lettere ed Arti*

2015-date: Fellow of the *Accademia Galileiana di Scienze Lettere ed Arti in Padova*

2013-date: Member of the European Molecular Biology Organization (EMBO)

2008-date: Member of the Academia Europaea, Section of Physiology and Medicine

SCIENTIFIC ACTIVITY

Coordinator of the Research Group on MITOCHONDRIAL CALCIUM SIGNALLING at the Department of Biomedical Sciences, University of Padua (Italy): <https://www.biomed.unipd.it/ricerca/aree-tematiche/mitochondrial-pathophysiology/mitochondrial-calcium-signalling>

Research keywords and abstract

5 keywords

cell signalling

calcium homeostasis

mitochondria

apoptosis/autophagy

muscle physiology

Abstract

The research interest of Prof. Rizzuto has been centered on the study of cellular signalling, with special focus on intracellular calcium homeostasis. He pioneered the use of molecularly engineered recombinant luminescent and fluorescent proteins for studying calcium homeostasis at the subcellular level. Subcellular targeting first of the luminescent protein aequorin of *Aequorea victoria*, and then of luciferase of *Photinus pyralis* and of the continuously expanding group of fluorescent probes based on green fluorescent protein (GFP) of *Aequorea victoria*, allowed major advancements in the study of calcium signalling, cellular metabolism and organelle morphology. With this methodological breakthrough, new biological concepts have been acquired, which include i) 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, ii) the occurrence and significance of signalling microdomains in the proximity of mitochondria, iii) the identification of the Golgi apparatus as an agonist-sensitive Ca²⁺ store, and iv) the major Ca²⁺ rises occurring under the plasma membrane upon cell stimulation, to cite a few. In 2011, using a combination of experimental approaches (in silico

search, reconstitution in planar lipid bilayers and electrophysiological characterization, expression and silencing in cultured cells, site-specific mutagenesis) he identified the mitochondrial calcium uniporter (MCU), the only fundamental component of the cellular calcium signalling machinery yet to be discovered. This result has opened, with an explosive pace, the molecular era of mitochondrial Ca^{2+} homeostasis, that combines the molecular insight into a multi-subunit protein complex, radically different from all other cellular channels, to the possibility of clarifying the role of mitochondria calcium homeostasis in the physiological regulation of tissues and in the pathogenesis of highly prevalent human diseases (neurodegenerative disorders, ischemic heart disease, cancer). Recent data on the role of MCU on muscle trophism and inflammasome control have provided a solid background to the possibility of targeting MCU with traditional and RNA-based drugs for treating pathological conditions such as age- and disease-related sarcopenia and inflammation-based diseases, such as inflammatory bowel diseases, lung fibrosis and atherosclerosis. Finally, with an approach similar to that employed for the discovery of MCU, also the long-sought and debated mitochondrial K_{ATP} channel, proposed to be a primary regulator of ischemic pre-conditioning, has been identified by Prof. Rizzuto's research team in 2019 and shown to control the volume of the mitochondrial matrix and the activity of respiratory complexes.

Research Projects - Principal Investigator

The research activity of prof. Rizzuto has been supported through the year by grants from the European Research Council (ERC Ideas Advanced grant - MitoCALCIUM: Mitochondrial calcium signalling: molecules, roles and pharmacological targeting), the EU FP programs, the National Institute of Health, the Italian Association for Cancer Research (AIRC), Telethon- Italy, the Italian Education and Health Ministries and the Cariparo and Cariplo bank foundations.

Bibliometry

ORCID: <https://orcid.org/0000-0001-7044-5097>

According to **Google Scholar** (User: OW0gQfUAAAAJ&hl): Total Citations: 76507.

H-Index: 124.

According to **Scopus** (Author ID 7005289262): Total Citations: 49356.

H-Index: 107.

According to **WoS** (Researcher ID B-6312-2008): Total number of citations: 45658.

H-index: 103.

Ranked 43rd in Top Italian Scientists (Biomedical Sciences)

https://www.topitalianscientists.org/TIS_HTML/Top_Italian_Scientists_Biomedical_Sciences.htm

Publications

298 full articles cited in Pubmed (<https://pubmed.ncbi.nlm.nih.gov/>)

<https://scholar.google.com/citations?user=OW0gQfUAAAAJ&hl=it&oi=ao>

Selected publications

5 publications (last 10 years)

1. S. Feno, F. Munari, D.V. Reane, R. Gissi, D.H. Hoang, A. Castegna, B. Chazaud, A. Viola*, R. Rizzuto*, A. Raffaello* (2021). The dominant negative mitochondrial calcium uniporter subunit MCUb drives macrophage polarization during skeletal muscle regeneration. *Sci. Signal.* 14(707):eabf3838.
2. A. Paggio, V. Checchetto, A. Campo, R. Menabò, G. Di Marco, F. Di Lisa, I. Szabo, R. Rizzuto*, D. De Stefani* (2019). Identification of an ATP-sensitive potassium channel in mitochondria. *Nature* 572:609-613.
3. M. Patron, V. Checchetto, A. Raffaello, E. Teardo, D. Vecellio Reane, M. Mantoan, V. Granatiero, I. Szabò, D. De Stefani* and R. Rizzuto* (2014) MICU1 and MICU2 finely tune the mitochondrial Ca²⁺ uniporter by exerting opposite effects on MCU activity. *Mol. Cell* 53:726-737.
4. A. Raffaello, D. De Stefani, D. Sabbadin, E. Teardo, G. Merli, A. Picard, V. Checchetto, S. Moro, I. Szabò, R. Rizzuto* (2013) The mitochondrial calcium uniporter is a multimer that can include a dominant-negative pore-forming subunit. *EMBO J.* 32:2362-76.
5. R. Rizzuto*, D. De Stefani, A. Raffaello, C. Mammucari (2012) Mitochondria as sensors and regulators of calcium signalling. *Nat. Rev. Mol. Cell Biol.* 9, 566-578.

*corresponding author

5 publications (whole career)

1. D. De Stefani, A. Raffaello, E. Teardo, I. Szabo, R. Rizzuto* (2011) A forty-kilodalton protein of the inner membrane is the mitochondrial calcium uniporter. *Nature* 476:336-340.
2. P. Pinton, A. Rimessi, S. Marchi, F. Orsini, E. Migliaccio, M. Giorgio, C. Contursi, S. Minucci, F. Mantovani, M. R. Wieckowski, G. Del Sal, P. G. Pelicci, R. Rizzuto* (2007) Protein kinase C beta and prolyl isomerase 1 regulate mitochondrial effects of the life-span determinant p66Shc. *Science* 315:659-663.
3. R. Rizzuto*, P. Pinton, W. Carrington, F. S. Fay, K. E. Fogarty, L. M. Lifshitz, R. A. Tuft, T. Pozzan* (1998) Close contacts with the endoplasmic reticulum as determinants of mitochondrial Ca²⁺ responses. *Science* 280:1763-1766.
4. R. Rizzuto*, M. Brini, M. Murgia, T. Pozzan* (1993) Microdomains with high Ca²⁺ close to IP₃-sensitive channels that are sensed by neighboring mitochondria. *Science* 262:744-747.
5. R. Rizzuto*, A. W. Simpson, M. Brini, T. Pozzan* (1992) Rapid changes of mitochondrial Ca²⁺ revealed by specifically targeted recombinant aequorin. *Nature* 358:325-327.

*corresponding author

Editorial Activity

Prof. Rizzuto routinely acts as reviewer for international scientific journals (*Nature*, *Science*, *Cell*, *J. Cell Biol.*, *EMBO J.*, *J. Biol. Chem.*, *Trends Cell Biol.*, etc.) and granting agencies (he is currently member of European Research Council and EMBO review panels).

Program Chairs/Organization Committee

- Gordon Research Conference on Calcium Signalling, Renaissance Tuscany Il Ciocco, Lucca, Italy, June 2013 (Chair: R. Rizzuto; vice-chair: D.I. Yule)
- Gordon Research Conference on Calcium Signalling, Colby Sawyer College- New London- NH, USA, June 2011 (chair. K. Foskett; vice-chair: R. Rizzuto)
- EMBO Workshop on “Calcium signaling and diseases”, Capri, Italy, September 2004 (organizers: E. Carafoli, R. Rizzuto)
- 12th International Symposium on Calcium Binding Proteins and Calcium Function in Health and Disease - Cavalese, Italy, February 2002 (organizers: E. Carafoli, R. Rizzuto, T. Pozzan)

Keynote speeches and lectures

Prof. Rizzuto gave >300 lectures at national and international meetings (including >20 plenary lectures) and seminars in Universities and Research Institutes.

MANAGEMENT ACTIVITIES

Research and academic management (1992-2015)

1992-1998: As “ricercatore” (tenured assistant professor) at the Department of Biomedical Sciences of the University of Padua, Dr. Rizzuto was the PI of research projects funded by Telethon, the Biomed program of the European Union and the University and Health Ministries, supervising the activity of junior researchers, fellows and PhD students.

1998-2008: As associate professor and then full professor at the Department of Experimental Medicine and Diagnostics of the University of Ferrara, Prof. Rizzuto coordinated a research group composed on average of 10 people, funded by the VII EU Framework Programme, Telethon, AIRC and the Ministries of University and Health. In addition to the projects of the research group, Telethon funded Prof. Rizzuto for the establishment in Ferrara of the Telethon Center for Cell Imaging (TCCI), an advanced microscopy center to host live cell experiments by Telethon researchers. Prof. Rizzuto was the founder and first coordinator of the Emilia-Romagna (ER)-GenTech network, funded by the Regional Program for Industrial Research, Innovation and Technological Research (PRRIITT), which gave rise to the Emilia-Romagna Technopoles, important research facilities still operating in the region. He was also a member of the University Research Council for two terms, and Dean of the Faculty of Pharmacy for one term. Before the enactment of Law 240/2010, the Faculties were responsible not only for the organization of degree courses, but also for the recruitment of university professors.

2008-2015. Back in Padua as a full professor at the Department of Biomedical Sciences, the activity of the research group continued with funding from Telethon, UE, AIRC, Cariparo and Cariplo foundations, and a size of the research group on average of 15 people. In 2011, Prof. Rizzuto was the recipient of an Advanced ERC grant of € 2.5 million (Mitocalcium project), which also allowed the first opening within the University of Padua of two academic positions (“ricercatore”) on external funds. From 2009 to 2015 prof. Rizzuto was Director of the Department of Biomedical Sciences (DSB) and from 2011 to 2015 member of the Academic Senate of the University of Padua. The DSB is a large Department, with 60 faculties and >300 research staff. In the Quality Assessment of Research of the University Ministry carried out during prof. Rizzuto’s chairmanship (VQR 2004-10), it was nationwide the most highly ranked department of the medical area (area 6), and the best performing department of Padua University. The department has a research grant portfolio of 5-6 M€/year from national and international competitive grants. Thanks to the departmental overhead, prof. Rizzuto activated common services for researchers, such as the animal care facility, an imaging center with one- and two-photon confocal microscopes and high-speed live cell imaging apparatuses, and a laboratory equipped for the handling of class II GMOs, which are still running within the department.

Rector of the University of Padua (2015-2021)

The University of Padua is large, comprehensive public University (70,000 students, >200 bachelor or master degree courses, spanning all the ST, LS and SH research areas). It was founded in 1222 and, site of free and open science, acknowledges among its scholars Galileo, Copernicus and the anatomists Morgagni, Vesalius, Fabrici d’Acquapendente and Harvey. Today, it is the largest enterprise of the Padua area, by employees and budget. It employs 2400 professors, 2500 technicians and administratives, and 3000 non-tenured post-graduates and research staff. The yearly budget is approx. 570 M€ (340 M€ from the Italian University Ministry, 230 M€ from other public and private sources and students’ tuitions). Prof. Rizzuto was elected Rector in 2015 with the program of further strengthening the research profile of the University. The following actions were undertaken:

- Academic recruitment of young researchers. A large recruitment plan was initiated, and 460 young faculties (“ricercatori”) were hired. This has been a huge investment, that allowed all departments to renew and expand their permanent academic staff and improved the scientific output and Ministry evaluation and performance-based funding of the University.
- Mentoring of high-profile scientists. ERC, and its strategies for promoting excellence in science, have been the benchmark of this policy. A new granting scheme was activated: Supporting Talents in Research@University of Padua (STARS@UNIPD) open to researchers (ERC Starting or Consolidator level) in Padua or moving to Padua, with grant proposal in ERC grant format and international review panels. Approx. 50 grants were awarded each year (150,000€/grant on average): by the end of the 2-year grant period, each grantee was committed to submit to ERC a grant proposal with the preliminary data obtained. In addition, a “Talents@UniPd” initiative searched and directly supported during all application phases promising PI candidates who intend to compete for the Annual Starting or Consolidator Grant Call of ERC having Padua as Host Institution. Finally, scientists awarded an ERC grant could be proposed by their departments for promotion to the higher professor level (Associate or Full Professor) with an extra recruitment budget provided by the University governance.

- Attraction of high-profile scientists. Also in this case, the ERC granting schemes have been the main reference, through a new recruitment scheme. At all times and with no number limitation, the University departments could propose the recruitment of an ERC awardee, also in this case fully covered by an extra budget provided by the University governance (i.e. additional to the recruitment budget assigned to departments in the yearly planning). Through this scheme, in the 6 years of the rector term of Prof. Rizzuto 20 ERC awardees moved to Padua to carry out their research, compared to none in the previous 5 years, broadening the research width of the University with talented scientists.
- Increase of international students, PhDs and faculties. Regarding students, during the rector term of Prof. Rizzuto the number of degree courses entirely held in English increased from 9 to 28 and now cover most University Schools. International communication of learning opportunities in Padua was greatly enhanced and foreign students are now assisted from the application to the integration in the University and city life. Consequently, the number of international students grew steadily in the last 6 years, from 250 first-year foreign students in 2014/15 (1.3% of total) to 2500 in 2021/22 (> 10% of total, 25% in master degrees). Similarly, international Ph.D. students also increased markedly, and now represent 17% of all Ph.D. students at the University. Finally, the University launched a recruitment scheme for professors (Italian or international) with permanent position in foreign institutions. A yearly competitive call opens in autumn, in which the departments propose international faculties for direct recruitment, with most of the cost (70-90%) covered by an extra budget provided by the University governance. In the 6 years of the Rector's term, 50 professors have been recruited from abroad through this scheme.
- In-house funding. A global, flexible research budget to departments (Integrated Departmental Research Budget) was established, allocated based on research performance, that the departments could use according to the requirements of their development plan (Ph.D. or post-doc fellowships, internal grants, start-up packages, facilities, etc.). In addition, a specific scheme was initiated for acquiring research instrumentations, with a yearly competitive call. In 2020, a special investment was made to finance the acquisition of "World Class Research Infrastructures" (WCRI), i.e. 5 high-cost instruments (€2.5 million each). After evaluation by an international committee, the projects for the acquisition of a 7 Tesla magnetic resonance imaging (UHI-7T-MRI), a single-cell molecular and metabolic imaging infrastructure (MINIATURE), a Quantum simulation and computation center (QCSC), a hyperextended reality infrastructure, for multidisciplinary use (HX R) and a laboratory for the study and mitigation of cultural heritage risk (SYCURI) were funded.
- Infrastructure and buildings. A global building plan was initiated to improve quality and amplitude of teaching and research spaces. The plan included a number of interventions, with a global cost of >200 M€. In this plan, three major new sites have been developed. The first has been the completion of a 10-year old project, transforming the former Geriatric Hospital of the city into the Literary campus of the university. Then, in a fruitful collaboration with other public institutions, the University acquired two other large compounds, the "Caserma Piave" from the Ministry of Defense and two pavilions of the Padua Exhibition from the local government. The first is a large (>50,000 m²) army barracks, built in the early XIX century on the historical site of a medieval cloister, that, via an elegant restoration project led by architect sir David Chipperfield, will now become the Social Sciences campus. The two pavilions in the

Exhibition, close to the Science and Technology departments, will be renovated and utilized as teaching facility (classrooms and labs) for the Engineering courses.

- University performance and rankings. According to the assessments of the Ministry and the ranking agencies, investments and budget management have proved effective for improving the University's results. The recent publication of the results of the Research Quality Assessment (VQR) 2015-2019, corresponding to the rectorate period of Prof. Rizzuto, and the selection of the 350 university departments admitted to the University Ministry "Departments of Excellence" competition have provided a very flattering picture. In the VQR 2015-2019, the University of Padua obtained among the public universities (excluding the Special Schools) the highest average grade both in profile A (established staff) and in profile B (promoted and newly hired), with the score of 0.76 and 0.81 respectively. In the Competition "Departments of Excellence", 29 departments of the University of Padua were selected (out of a total of 32), of which 22 with the maximum score (ISPD 100), in both cases the highest absolute value among the Universities. In the overall evaluation of teaching, research and management, the University of Padua has received the A score in the first periodic assessment "accreditamento") of ANVUR (the Ministry evaluation agency). International evaluations gave a result that is consistent with that of the national assessment. In the Nature index, the University of Padua ranks 4th among Italian institutions (after the National Institute for Nuclear Physics, INFN, the National Research Council, CNR and the Scientific Institutes for Research, Hospitalization and Healthcare, IRCCS) and 1st among Italian Universities. In all rankings of the major international agencies, the University of Padua has greatly improved its performance (e.g. Times Higher Education from 325 in 2016 to 275 in 2020, QS from 338 to 216).

President of the National Center for Gene Therapy and Drugs based on RNA technology (2021-date)

Following the publication by the University Ministry (MUR) of a competitive call for the establishment of 5 National Centers (PNRR Mission 2 "Education and Research", Component 2 "From Research to Enterprise, Investment 1.4 "Potentiation of research structures and creation of national champions of R&D on some Key Enabling Technologies), the University of Padua decided to act as proposer of a National Center on theme 3 ("Development of gene therapy and drugs with RNA technology"), asking prof. Rizzuto to build the network, design the scientific content and coordinate the recruitment of the partners and the writing of the proposal. The requirement of the call was to build highly competitive large National Centers, with a critical mass of at least 250 researchers, operating with a hub, that coordinates the global research activity, guaranteeing and reporting to MUR the attainment of research and administrative milestones, and >5 spokes that include public and private partners and carry out the proposed research. The National Centers can include up to 25 MUR-controlled public entities (i.e. Universities and Research Centers) and up to 24 other public and private entities. Budget allocation must follow the requirements of the PNRR (> 40% allocated to the 8 regions of the South of Italy, gender balance in recruitment, definition and clear allocation to fundamental and industrial research, participation to the climate and digital aims of European research). Specifically, the Center on gene therapy and drugs with RNA technology (CN3) was planned with 10 spokes, either "vertical", i.e. with the goal of bringing biomedical research to the development of specific drugs in key areas,

or “horizontal”, i.e. focused on improving the novel technologies of the National Center, as detailed below. At first, research institutions with strong research activity on the topic of the planned spokes were identified and asked to lead the spoke and participate in the steering committee of the grant proposal. In detail, topics and leaders of the spokes are as follows. The 5 vertical spokes are focused on genetic diseases (spoke 1, University of Modena and Reggio Emilia), cancer (spoke 2, Sapienza University in Rome), neurodegenerative diseases (spoke 3, Italian Institute of Technology, IIT), metabolic and cardiovascular diseases (spoke 4, University of Padua) and inflammatory and infectious diseases (spoke 5, University of Siena). The 5 horizontal spokes are focused on RNA/DNA chemistry (spoke 6, National Research Council, CNR), advanced biocomputing (spoke 7, University of Bari), nucleic acid delivery (spoke 8, Federico II University in Naples), pharmacology and biosafety (spoke 9, University of Milan) and clinical applications of gene therapy (spoke 10, Bambino Gesù Hospital). Then, an extensive search of expertise and groundbreaking projects in the field of interest of the National Center was carried out, that allowed the recruitment of top scientists from the biomedical and clinical sciences, chemistry and material sciences. Overall, >800 high-profile scientists were included in the proposal (6 scientists with a Scopus h-index >100, 6 with an h-index >90, >100 senior investigators with an h-index >50, >200 with h-index >40, and 30% early career researchers). Based on the scientific selection, 24 public Universities, CNR and 7 non MUR-controlled research entities were invited and accepted to join the CN3. Then, CN3 was presented to national and international companies and a list of private partners was selected based on the research priorities and the commitment and potential contribution to activities. These partners include the largest Italian bank (Intesa San Paolo) and 16 pharma companies, ranging from the international leaders of the field (Pfizer, BioNTech, AstraZeneca, Sanofi, Novartis) to major Italian companies (Chiesi, Bracco, Dompè, Stevanato). It should be noted that each partner agreed not only to participate in the research activities of CN3, but also to contribute a yearly fee (100 K€ for research entities, 200 K€ for large companies, 50 K€ for SME). The proposal was submitted by the deadline of February 15th, 2022, positively evaluated by an international review panel and, after revision of the proposal on the basis of the reviewers’ critiques, admitted to negotiation with the University and Economy Ministries (MUR and MEF) at the end of May. At the positive outcome of negotiation, with the assignment of a budget by MUR of 320,036,606 €, on June 7th, 2022 the CN3 partners started the legal entity of the Hub (the foundation “National Center on gene therapy and RNA-based drugs”). The assembly of partners nominated prof. Rizzuto as President of the Foundation.