



## Salvador Moncada



**Date of Birth** 3 December 1944

**Place** Tegucigalpa (Honduras)

**Nomination** 28 September 2016

**Field** Biology - Medicine

**Title** Professor

### Most important awards, prizes and academies

Foreign Member of the National Academy of Sciences of the United States of America (1994); Fellow of the Royal College of Physicians, London (1994), and Honorary Fellow of University College, London (1999). He was elected a Fellow of the Royal Society (FRS) in 1988.

He has received honorary degrees from more than twenty universities, including Honorary Degree of Doctor of Science, Mount Sinai School of Medicine, New York, USA (1995); Degree of Doctor "Honoris Causa" of the University Pierre & Marie Curie, Paris, France (1997) and Honorary Degree of Doctor of Science of the University of Edinburgh, Scotland (2000).

His prizes and distinguished lectures include: The VIII Gaddum Memorial Lecture, British Pharmacological Society (1980); The Ulf von Euler Memorial Lecture, Karolinska Institute, Stockholm, Sweden (1991); The Paul Dudley White Lecture, American Heart Association, Anaheim, California, USA (1991); The Royal Medal of the Royal Society, UK (1994); The Gregory Pincus Memorial Lecture, the Worcester Foundation for Biomedical Research, Massachusetts, USA (1996); The Louis and Artur Lucian Award (jointly with Prof. R. Furchgott), McGill University, Montreal, Canada (1997); The Bayliss-Starling Prize Lecture to the Physiological Society, UK (2000); The Gold Medal of the Royal Society of Medicine, UK (2000); Le Grand Prix Annuel Lefoulon-Delalande, from the Institut de France, Paris (2002); the Croonian Lecture at the Royal Society, London, UK (2005), the Debrecen Award for Molecular Medicine from the University of Debrecen, Hungary (2011)[13] and The Dohme Lecture, The Johns Hopkins University School of Medicine, Baltimore (2010).

In 2010 he also received a Knighthood from Her Majesty the Queen in recognition of his services to Science. In 2013 he was awarded the Ernst Jung Gold Medal for Medicine (Ernst Jung Prize).

### Summary of scientific research

Salvador Moncada, MD, obtained his PhD in the early 1970s at the Royal College of Surgeons in London, where he contributed to the discovery that aspirin-like drugs inhibit prostaglandin biosynthesis, thus accounting for their analgesic, anti-pyretic and anti-inflammatory actions.

In 1975 he joined the Wellcome Research Laboratories where, as Head of the Department of Prostaglandin Research, he initiated the work leading to the discovery of the enzyme thromboxane synthase and the vasodilator prostacyclin. This work contributed to the understanding of how low doses of aspirin prevent cardiovascular episodes such as myocardial infarction and stroke. He was Director of Research at the Wellcome Research Laboratories from 1986 until 1995, during which time he oversaw the discovery and development of a number of drugs, including lamotrigine (anti-epileptic), zomig (anti-migraine), atovaquone (anti-malarial) and the initiation of the project which led to the finding and development of lapatinib (anti-cancer).

In 1985 he began a project that led to the identification of nitric oxide (NO) as the biological mediator formerly known as endothelium-derived relaxing factor. He elucidated the pathway of the synthesis of NO from the amino acid L-arginine and discovered many of the biological activities of this novel mediator. His finding that NO is generated in the central nervous system led him to propose that the L-arginine: NO pathway is a widespread transduction mechanism for regulating cell function and communication.

In 1996 Prof. Moncada moved to University College London to establish and direct the Wolfson Institute for Biomedical Research (originally known as the Cruciform Project). The aim of this Institute has been to establish a centre of excellence in biomedical research that provides an interface between academia and industry, thus establishing one of the earliest units for translational research in the UK. This approach has led to the setting up of a number of spin-out companies, including Ark Therapeutics (vascular disease and cancer), Arrow Therapeutics (anti-infective drugs), CereXus (neuroscience), Inpharmatica (bioinformatics) and ProAxon (sodium channel blockers).

At the invitation of the Spanish Government, between 1999 and 2004 Professor Moncada conceived, designed and developed the Centro Nacional de Investigaciones Cardiovasculares (CNIC) in Madrid.

In the last decade his work has focused on the interaction between NO and cytochrome c oxidase, the terminal enzyme of the mitochondrial electron transport chain. This work has established the role of NO as a physiological regulator of cell respiration and a cell signalling molecule in response to stress. In addition, he has shown that interactions between NO and oxygen at the level of cytochrome c oxidase might also initiate pathophysiology. His recent finding that NO is involved in mitochondrial biogenesis has implications for the understanding of metabolic syndrome, type-2 diabetes and obesity.

His interest in glycolysis has led him, in recent years, to the identification of a molecular mechanism that coordinates cell proliferation with the provision of the metabolic substrates required for this process. This research has significant implications for the understanding of normal and abnormal cell proliferation, for example in cancer.

From 2010 to 2013 he ran an independent VIB-K.U. research group in the VIB Vesalius Research Center in Leuven, Belgium. The research team, which he ran concurrently with his laboratory at the WIBR, focused on basic research to unravel the molecular basis and explore the therapeutic potential of the link between metabolism and cell proliferation.

In October 2013 Prof Moncada became Emeritus Professor of Experimental Biology and Therapeutics at University College London and Professor of Translational Medicine and Strategic Advisor at the University of Manchester. In January 2014 he took on the role of Institute Director of Cancer Sciences, Faculty of Medical and Human Sciences, University of Manchester and in August 2016 he became Cancer Domain Director

Prof. Moncada's research has had a major impact, as shown by his standing in the international citation indexes and his acknowledgement as the most cited UK scientist in biomedicine in the 1990s.

### **Main publications**

Moncada is the author of over 800 peer-reviewed papers and highly cited reviews, including his latest ones: Carré, J., Singer, M. and Moncada, S. (2006). Nitric oxide. In: Mechanisms of Sepsis-Induced Organ Dysfunction and Recovery. Ed. Abraham, E. and Singer, M., Springer, Heidelberg, pp. 77-95; Valerio, A., Cardile, A., Cozzi, V., Bracale, R., Tedesco, L., Pisconti, A., Palomba, L., Cantoni, O., Clementi, E., Moncada, S., Carruba, M.O. and Nisoli, E. (2006). TNF- $\alpha$  downregulates eNOS expression and mitochondrial biogenesis in fat and muscle of obese rodents. *J. Clin. Invest.*, 116, 2791-2798; Moncada, S. (2006). Sir John Robert Vane, a biographical memoir. *Biogr. Mems. Fell. R. Soc.*, 52, 401-411; Palacios-Callender, M., Hollis, V., Frakich, N., Mateo, J. and Moncada, S. (2007). Cytochrome c oxidase maintains mitochondrial respiration during partial inhibition by nitric oxide. *J. Cell Sci.*, 120, 160-165; Diaz-Hernandez, J.L., Moncada, S., Bolaños, J.P. and Almeida, A. (2007). Poly(ADP-ribose) polymerase-1 protects neurons against apoptosis induced by oxidative stress. *Cell Death and Differentiation*, 14, 1211-1221; Nisoli, E., Clementi, E., Carruba, M.O. and Moncada, S. (2007). Defective mitochondrial biogenesis: A hallmark of the high cardiovascular risk in the metabolic syndrome? *Circ. Res.*, 100, 795-806; Funes, J.M., Quintero, M., Henderson, S., Martinez, D., Qureshi, U., Westwood, C., Clements, M.O., Bourboulia, D., Pedley, R.B., Moncada, S. and Boshoff, C. (2007). Transformation of human mesenchymal stem cells increases their dependency on oxidative phosphorylation for energy production. *Proc. Natl. Acad. Sci.*, 104, 6223-6228; Galkin, A., Higgs, A. and Moncada, S. (2007). Nitric oxide and hypoxia. In: *Essays in Biochemistry – Oxygen sensing and hypoxia-induced responses*, ed. C. Peers, Portland Press, London, 43, 29-42; Erusalimsky, J.D. and Moncada, S. (2007). Nitric oxide and mitochondrial signaling. From physiology to pathophysiology. *Arterioscler. Thromb. Vasc. Biol.*, 27, 2524-2531; Galkin, A. and Moncada, S. (2007). S-Nitrosation of mitochondrial complex I depends on its structural conformation. *J. Biol. Chem.*, 282, 37448-37453; Palacios-Callender, M., Hollis, V., Mitchison, M., Frakich, N., Unitt, D. and Moncada, S. (2007). Cytochrome c oxidase regulates endogenous nitric oxide availability in respiring cells: A possible explanation for hypoxic vasodilation. *Proc. Natl. Acad. Sci. USA*, 104, 18508-18513; Lafuente, N., Matesanz, N., Azcutia, V., Romacho, T., Nevado, J., Rodríguez-Mañá, L., Moncada, S., Peiró, C. and Sánchez-Ferrer, C.F. (2008). The deleterious effect of high concentrations of D-glucose requires pro-inflammatory preconditioning. *J. Hypertension*. 26, 478-485; Victor, V.M., Nuñez, C., D'Ocón, P., Taylor, C.T., Esplugues, J.V. and Moncada, S. (2009). Regulation of oxygen distribution in tissues by endothelial nitric oxide.

Circ. Res., 104, 1178-1183; Herrero-Mendez, A., Almeida, A., Fernández, E., Maestre, C., Moncada, S. and Bolaños, J. (2009). The bioenergetic and antioxidant status of neurons is controlled by continuous degradation of a key glycolytic enzyme by APC/C-Cdh1. *Nature Cell Biol.*, 11, 747-752; Colombo, S.L. and Moncada, S. (2009). AMPK $\alpha$ 1 regulates the antioxidant status of vascular endothelial cells. *Biochem. J.*, 421, 163-169; Taylor, C.T. and Moncada, S. (2010). Nitric oxide, cytochrome c oxidase, and the cellular response to hypoxia. *Arterioscler. Thromb. Vasc. Biol.*, 30, 643-647; Bolaños, J.P., Almeida, A. and Moncada, S. (2009). Glycolysis: a bioenergetic or a survival pathway? *Trends in Biochem. Sci.*, 35, 145-149; Almeida, A., Bolaños, J.P. and Moncada, S. (2010). E3 ubiquitin ligase APC/C-Cdh1 accounts for the Warburg effect by linking glycolysis to cell proliferation. *Proc. Natl. Acad. Sci.*, 107, 738-741; Unitt, D.C., Hollis, V.S., Palacios-Callender, M., Frakich, N. and Moncada, S. (2010). Inactivation of nitric oxide by cytochrome c oxidase under steady-state oxygen conditions. *Biochim. Biophys. Acta.*, 1797, 371-377; Moncada, S. (2010). Mitochondria as pharmacological targets. *Br. J. Pharmacol.*, 160, 217-219; Colombo, S.L., Palacios-Callender, M., Frakich, N., De Leon, J., Schmitt, C.A., Boorn, L., Davis, N. and Moncada, S. (2010). Anaphase-promoting complex/cyclosome-Cdh1 coordinates glycolysis and glutaminolysis with transition to S phase in human T lymphocytes. *Proc. Natl. Acad. Sci. USA*, 107, 18868-18873; De Palma, C., Falcone, S., Pisoni, S., Cipolat, S., Panzeri, C., Pambianco, S., Pisconti, A., Allevi, R., Bassi, M.T., Cossu, G., Pozzan, T., Moncada, S., Scorrano, L., Brunelli, S. and Clementi, E. (2010). Nitric oxide inhibition of Drp1-mediated mitochondrial fission is critical for myogenic differentiation. *Cell Death Diff.*, 17, 1684-1696; Tudzarova, S., Colombo, S.L., Stoeber, K., Carcamo, S., Williams, G.H. and Moncada, S. (2011). Two ubiquitin ligases, APC/C-Cdh1 and SKP1-CUL1-F(SCF)- $\beta$ -TrCP, sequentially regulate glycolysis during the cell cycle. *Proc. Natl. Acad. Sci., USA*, 108, 5278-5283; Colombo, S. L., Palacios-Callender, M., Frakich, N., Carcamo, S., Kovacs, I., Tudzarova, S. and Moncada, S. (2011). Molecular basis for the differential use of glucose and glutamine in cell proliferation as revealed by synchronized HeLa cells. *Proc. Natl. Acad. Sci. U.S.A.*, 108, 21069-21074; Moncada, S., Higgs, E.A. and Colombo, S.L. (2012). Fulfilling the metabolic requirements for cell proliferation. *Biochem. J.*, 446, 1-7; Moncada, S. (2014). The vascular endothelium. *Anales de la Facultad de Medicina, Universidad Nacional Mayor de San Marcos, Perú* 75, (4), 333-338; Peiro, C., Romancho, T., Azcutia, V., Villalobos, L., Fernandez, E., Bolanos, J.P., Moncada, S., and Sanchez-Ferrer, C.F. (2016). Inflammation, glucose, and vascular cell damage: the role of the pentose phosphate pathway. *Cardiovascular Diabetol*, 15, (1):82.