Distinguished Visitor Programme

Prof Salvador Moncada
Director, Wolfson Institute for Biomedical Research

Biography

Prof Salvador Moncada was born in Tegucigalpa (Honduras) in 1944 and graduated in Medicine at the University of El Salvador in 1970. In 1973 he earned a Ph.D. degree in Pharmacology at the University of London, where he became Doctor of Science 10 years later. He returned to the University of Honduras in 1974-1975 as Associate Professor of Pharmacology and Physiology and then joined the Wellcome Research Laboratories in England first as Section Leader of the prostaglandin research group, and then as Head of the department of prostaglandin research. In 1984 he became Director of Therapeutic Research Division, and in 1986 Director of Research of the Wellcome Research Laboratories. Since 1995 he is the Director of the Wolfson Institute for Biomedical Research of the University College London.

Moncada's work has been instrumental in the discovery of prostacyclin, and of the enzyme. Dr. Moncada's research interests have always been centered on the pharmacological effects of vasoactive substances, of which nitrogen monoxide (the NO radical) has been his favorite topic for about 20 years. He has been responsible for a large portion of the fundamental discoveries on this very important (and very popular) second messenger, beginning with the demonstration of its identity with the endothelium-derived relaxing factor (EDRF) and with the clarification of the mechanism of its formation. The area of NO action has now undergone a phenomenal expansion, and Dr. Moncada has been a key actor in most of its aspects.

The work of Dr. Moncada has been recognized with numerous international prizes and distinctions, including the Atomo d'Oro Prize of the Roman Academy of Medical and Biological Sciences, the Amsterdam Prize for Medicine, the Roussel-Uclaf Prize, the Royal Medal of the Council of the Royal Society, the Ciba Award for Hypertension Research, the Dale Medal, the Gold Medal of the Royal Society of Medicine. Dr. Moncada is the recipient of 15 Honorary degrees, and is a foreign member of the National Academy of Sciences.
Lecture Abstract

4 May 2002

"Nitric Oxide: from discovery to the clinic"

In 1987 it was discovered that vascular endothelial cells release nitric oxide (NO) and its generation from the amino acid L-arginine was subsequently established. NO is formed by a family of enzymes, the NO synthases, and is involved in many physiological functions. Its formation in vascular endothelial cells maintains a vasodilator tone that is essential for the regulation of blood flow and pressure. A decrease in the synthesis or actions contributes to the development of some vascular pathologies, including hypertension, vasospasm and atherosclerosis.

NO is also synthesized in the central nervous system, where it acts as a neuromediator with several physiological functions, including the formation of memory. In the peripheral nervous system, NO is now known to be the mediator released by a widespread network of nonadrenergic, noncholinergic nerves that mediate some forms of neurogenic vasodilation and regulate certain gastrointestinal, respiratory and genitourinary functions. All these physiological actions of NO are mediated by activation of the soluble guanylate cyclase in target cells.

In addition, NO is generated in large quantities during host defence and immunological reactions. When NO is released in this way it contributes to the development of certain pathologies, including septic shock and some forms of inflammation.

One way in which NO may be transformed from a physiological mediator to a pathophysiological agent may be through its actions on mitochondrial function. At low, physiological concentrations NO inhibits cell respiration in a reversible manner which is competitive with oxygen. At higher concentrations it irreversibly inhibits enzymes in the respiratory cycle, either directly or through interaction with superoxide anion leading to the generation of peroxynitrite. Increased understanding of the biochemical actions of NO and the role it plays in mitochondrial function and gene expression will doubtless lead to novel therapeutic applications.