

obituary

Sir John Vane: Field Marshall in the fight against disease

Barry Whyte, barry@rochat-pr.ch

'...I think I know how aspirin works.'

Sir John Vane, who shared the Nobel Prize for Medicine in 1982 for his work on aspirin and the subsequent discovery of prostacyclin, has died at the age of 77. In a career spanning over 40 years of research, Vane made many outstanding contributions that paved the way for new treatments for cardiovascular disease, pain and chronic inflammation.

In 1971, Vane discovered that aspirin and related drugs act by inhibiting the synthesis of a group of lipid mediators called prostaglandins. Not long afterwards, he and his colleagues were the first to discover prostacyclin – a key prostaglandin that dilates blood vessels and inhibits blood clotting. As Director of Research and Development at the Wellcome Foundation, London, UK, he played a significant role in the development of many commercial drugs including Tracrium (muscle relaxant), Flolan (anticoagulant), Zovirax (antiviral) and Lamictal (for the treatment of epilepsy). The William Harvey Research Institute, which he founded and directed for over 11 years, referred to him as 'our Field Marshall in the fight against disease'.

Adventures and excursions in bioassays

Vane was born in Tardebigg, Worcestershire, UK, in 1927. His father was a son of immigrants from Russia and his mother came

from a local farming community. At the early age of 12, he received a chemistry set and began experimenting in his mother's kitchen. After a minor explosion with limited structural damage, he was quickly relocated to a new wooden shed that his father had built in the garden. Here, his chemical experimentation could rapidly expand into new directions without any immediate risk to family and friends.

After attending King Edward VI High School at Edgbaston, he went on to study chemistry at Birmingham University, UK. Disappointed as a result of the lack of scope to perform experiments in his university course, he was somewhat discouraged by his career path. When he was asked what he wished to do after graduation, he replied: 'Anything but chemistry'.

In 1946, Vane decided to pursue pharmacology under the tutorage of Oxford pharmacologist Professor Harold Burn. It was Burn who taught him the principles and practice of biological assays, techniques that were to have a major impact on Vane's later contributions to science. 'With extraordinary simplicity and convenience... bioassay distinguishes between the important biologically active compounds and their closely related but biologically unimportant metabolites'.

Dissecting the mode of action of aspirin

Around 1970, Vane was working at the Royal College of Surgeons of England in a laboratory



with a large interest in the activities of hormone action and prostaglandins. After some initial experiments, Vane came up with the idea that aspirin might be interfering with prostaglandin synthesis. After one particular weekend thinking about recent results, he said to his colleagues: 'I think I know how aspirin works' [1] and he set about testing his hypothesis using a bioassay. He homogenized some guinea-pig tissue, removed the cells by centrifugation and divided the remaining liquid fractions into test tubes. 'To some of the tubes was added aspirin... By the end of the day I was convinced that aspirin strongly inhibited the formation of prostaglandins from arachidonic acid.' Vane had discovered one of aspirin's main secrets. This crucial discovery is at the centre of how aspirin prevents blood clots and how it considerably reduces the likelihood of heart attacks and strokes.

From prostacyclin to ACE inhibitors

In 1973, Vane accepted the position of Group Research and Development Director of the Wellcome Foundation. Initially, some friends raised concern as to whether he should

obituary

pursue his career in the private sector. However, he himself had no such reservations. Sir Henry Dale, one of the great influences on British pharmacology and on Vane's scientific work, had made a similar transition in the early days of the Wellcome Foundation. From the start, Vane was convinced that good science was not confined to academic laboratories.

In 1976, Vane and colleagues discovered prostacyclin, the prostaglandin that relaxes blood vessels and inhibits the clotting of red blood cells. Prostacyclin went on to be one of the most widely prescribed drugs for the treatment of pulmonary hypertension. Vane also initiated research programs that led to new treatments for heart and vascular disease, including angiotensin-converting enzyme inhibitors (ACE inhibitors), widely used to treat high blood pressure, heart problems and other vascular diseases.

Vane received a knighthood in 1984 and left the Wellcome Foundation one year later to become the founder and director of the William Harvey Research Institute at St. Bartholomew's Hospital (London, UK). Today, the William Harvey Research Institute has over 150 researchers and is one of the leading

SIR JOHN VANE'S CAREER HIGHLIGHTS

1951–1953	Stothert Research Fellow of the Royal Society, Oxford University, UK
1953–1955	Assistant Professor of Pharmacology, Yale University, CT, USA
1955–1961	Senior Lecturer in Pharmacology, Royal College of Surgeons, London University, UK
1961–1965	Reader in Pharmacology, Royal College of Surgeons, London University, UK
1966–1973	Professor of Experimental Pharmacology, London University, UK
1974	Fellow of the Royal Society
1973–1985	Research and Development Director, Wellcome Foundation, UK
1982	Nobel Prize in Physiology or Medicine
1984	Knighted
1986–1990	Director, William Harvey Research Institute, St Bartholomew's Hospital, London, UK
1990–1997	Director-General, William Harvey Research Institute, St Bartholomew's Hospital, London, UK
1997–2004	Honorary President, William Harvey Research Institute, St Bartholomew's Hospital, London, UK

centres for pharmacological research in the UK. In 1997, Vane retired but remained the honorary president of the institute's charitable arm, the William Harvey Research Foundation.

Sir John Vane was a remarkable experimentalist who played a major role in the battle against disease. He was known for his generous personality and commitment to science. He also took every step possible to encourage the development of new scientific talent. Vane regularly supported the Biomedical Education Research Trust by teaching school children about the need for medical research and he publicly supported the humane use of animals in medical research. He passionately believed that by directing medical research at the cause of disease, more effective treatments could be developed and introduced.

Sir John Vane died on Friday 19th November 2004.

Reference

- 1 Vane, J. (1993) Adventures and excursions in bioassay: the stepping stones to prostacyclin. In *Nobel Lectures in Physiology or Medicine 1981–1990* (Frängsmyr, T. and Lindsten, J. eds), World Scientific Publishing Company, Singapore

Barry Whyte

Rochat & Partners,
Rue Du-Roveray 12,
Geneva,
Switzerland
e-mail: barry@rochat-pr.ch