Peter Harris was an influential international statesman in cardiology. A science scholar at King’s College, London, UK, Harris trained in medicine at Kings College Hosp., qualifying in 1946. During house appointments at King’s and the Brompton Hosp., he obtained his MD in 1951, winning the university gold medal and a PhD in 1955. He was appointed lecturer, in 1957, and reader in medicine, in 1962, at Birmingham University. In 1966, he was appointed the first Simon Marks’ Professor of Cardiology at the Cardiothoracic Institute and Director of the Institute of Cardiology, in the Univ. of London.

His career, which was dedicated to exploring the cardiovascular system and the origins of heart disease, can be viewed as three chapters. During the 1950’s and early 1960’s, he was in the mainstream of research, and used established methods of haemodynamic measurements to explore cardiac output and pulmonary blood flow and the metabolism of the heart muscle. [During]…the second stage of his career …his research into the heart muscle turned to experiments at the cellular and molecular level. In 1970, Harris organized a meeting of …an international study group for research in cardiac metabolism, which resulted in the publication of one of the most influential works on cardiology: Calcium and the Heart. The third element to Harris’s career involved his fascination with the evolution of the cardiovascular and related systems. In a series of essays in 1983, he traced the way that the origins of clinical heart failure might lie in ancient reflexes. His study of the right ventricle of the heart and the blood flow to the lungs of yaks showed they had adapted genetically to high altitude by eliminating the vasoconstrictor response due to reduction of oxygen.

Away from the laboratory, he was a talented musician and artist, and he showed a leaning toward satirical writing. His wife Francesca survives him.

Prof Harding’s interests have centred on the function of the cardiac myocyte from the failing human heart since 1987, when she developed a method for the reliable isolation of intact myocytes from human atria and ventricles and established the suitability of the myocyte preparation (both human and animal) for constructing concentration-response curves to pharmacological agents. She started work on beta-adrenoceptor mechanisms during her first post-doctoral position, which was supervised by Professor Peter Harris.

Since that time, she has defined the main contractile deficits in myocytes from failing human heart, showing that the frequency response is lost and that stimulation through the beta-adrenergic receptor (βAR) is depressed. Prof Harding was among those providing evidence for a role of SERCA2a loss and Gi upregulation in these phenomena. Studies on animal models of βAR desensitisation or overexpression, hypertrophy and heart failure, as well as adeno/viral/AAV transfection of animal myocytes in vitro and in vivo, have unravelled processes underlying the alterations seen in human cardiomyocytes in heart failure. She was part of the first wave of a clinical trials attempting to find a gene therapy for heart failure using these data.

More recently, she has been leading the British Heart Foundation Centre for Cardiac Regeneration at Imperial College London, with partners in Glasgow, Westminster, Hamburg, and Nottingham. The Centre aims to generate new cardiac muscle in damaged hearts, with strategies including engineered heart tissue from human pluripotent stem cells. These cells and constructs are also being used for disease modelling, with CRISPR/Cas9 gene editing to produce isogenic lines.

A continuing interest in the βAR system in failing human heart has led to studies on subcellular compartmentation of the β1AR and β2AR and its alteration in disease. With Slava Nikolaev (Hamburg) and Julia Gorelik (Imperial) the spatial confinement of the β2AR -cAMP signal through phosphodiesterase localisation has been defined. The difference between apical and basal cardiomyocytes in the degree of compartmentation has recently been described. The ability of both beta-agonists such as adrenaline and some beta-blockers to drive the β2AR from Gs to Gi signalling was also discovered.

These findings gave Prof Harding insight into the mechanisms of Takotsubo syndrome or Stress Cardiomyopathy, in which acute severe heart failure follows a natural or iatrogenic catecholamine stimulus. In the lecture she will describe the current understanding of this syndrome clinically and show that the characteristic apical ballooning can be reproduced by a model where high adrenaline gives a switch from Gs to Gi coupling. She will discuss recent findings for a sensitising role of two microRNAs for this syndrome, linking the effect to previous anxiety and stress disorders. Data from these experiments demonstrates how the microRNA changes interact with the compartmentation and differential expression of β2AR signalling pathway components to produce regional effects on the heart.