

Summary of the Dame Commander Frances Ashcroft's Scientific Research

Frances Ashcroft discovered the KATP channel expressed in β cells which is a critical component of the signaling pathway that stimulates insulin secretion in response to elevated blood glucose. She discovered that closure of this channel by glucose metabolism into ATP plays an essential role in insulin release. She provided many mechanistic insights into the molecular operation of the channel, and its regulation by nucleotides and sulphonylurea drugs. In a formidable collaboration with Andrew Hattersley, a previous Luft Prize winner, she showed that gain-of-function mutations in KATP channel genes cause neonatal diabetes, and elucidated the underlying molecular mechanisms. This led to their discovery that these patients are well treated with sulphonylureas and that they do not need to be treated with insulin. This work has revolutionized the treatment of neonatal diabetes and over 90% of patients have switched from insulin injections to oral sulphonylurea therapy. This has greatly improved their clinical condition and quality of life. Ashcroft's recent studies have showed that hyperglycaemia in diabetes impairs oxidative metabolism in beta-cells, by altering expression of numerous metabolic genes. This is mediated by a glycolytic metabolite (not glucose itself) and blocking glucose metabolism prevents the deleterious effects of hyperglycaemia on the beta-cell. This suggests a novel approach to preventing beta-cell decline in type 2 diabetes. In addition to her scientific accomplishments Ashcroft is a prominent and acclaimed author. She wrote an important text book, Ion Channels in Health and Disease and has also written several acclaimed books for the lay public. In her book The Spark of Life, Ashcroft explains how electrical signals are essential for life. In Life at the Extremes, Ashcroft weaves stories of extraordinary feats of endurance with historical material and the latest scientific findings as she investigates the limits of human survival and the remarkable adaptations that enable us to withstand extreme conditions.