Hypoglycaemia in diabetes is still a frequent concern for people with diabetes and carries with it the increased risk of heart attacks, strokes and brain damage. The energy sensing enzyme, AMP-activated protein kinase (AMPK), is activated by glucose deprivation and has emerged as a critical regulator of whole body metabolism over the past 15 years, partly via central mechanisms. This talk will present findings that AMPK plays an important role in glucose-sensing cells including pancreatic beta cells and hypothalamic glucose excited neurons. We will also present data demonstrating that a novel brain permeable AMPK activator amplifies the counterregulatory response to hypoglycaemia in rats.