“Cardiovascular KATP: The Surprises – and Diseases – Keep on Coming”

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Abstract
ATP-sensitive potassium (KATP) channels were first discovered in the heart 30 years ago. Reconstitution of KATP channel activity by coexpression of members of the pore-forming inward rectifier gene family (Kir6.1, KCNJ8, and Kir6.2 KCNJ11) with sulfonylurea receptors (SUR1, ABCC8, and SUR2, ABCC9) of the ABCC protein sub-family, has led to the elucidation of many details of channel gating and pore properties. In addition, the essential roles of Kir6.x and SURx subunits in generating cardiac and vascular KATP2 and the detrimental consequences of genetic deletions or mutations in mice have been recognised. There has been a paucity of defined roles of KATP subunits in human cardiovascular diseases, although there are reports of association of a Kir6.1 variant with the J-wave syndrome in the electrocardiogram, and isolated studies have reported association of loss of function mutations in SUR2 with atrial fibrillation and heart failure. New studies convincingly demonstrate that mutations in the SUR2 gene are associated with Cantu syndrome, a complex multi-organ disorder characterized by multiple organ symptoms, but including patent ductus arteriosus, cardiomegaly, pericardial effusion, and lymphoedema. Through animal models and human clinics, we have now gained considerable new insights to previously unconsidered consequences of KATP channel overactivity in the cardiovascular system.