P023 Roles for ATP-sensitive potassium channels on dense core secretory vesicles but not mitochondria in pancreatic β-cells

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The distribution and role of intracellular ATP-sensitive potassium channel (K_{ATP}) subunits in pancreatic beta cells is still poorly defined. Nycodenz™ density gradient fractionation of MIN6 pancreatic beta cells revealed that >90 % of total cellular SUR1 and >30 % of Kir6.2 immunoreactivity was associated with dense core secretory vesicles and both subunits were present in immunoadsorbed or FACS-sorted, phogrin-EGFP-labelled vesicles. By contrast, Kir6.2 and SUR1 immunoreactivity were essentially undetectable in mitochondrial fractions.

Monitored with recombinant targeted aequorins in permeabilised MIN6 cells, diazoxide (50–100 microM) slightly increased Ca^{2+} uptake into mitochondria. This effect was abolished by atractyloside and was likely due to inhibition of adenine nucleotide translocase activity and increased mitochondrial membrane potential. Whereas diazoxide had no effect on Ca^{2+} uptake into dense core vesicles, tolbutamide (500 μM) slightly accelerated this process. We conclude that "classical" K_{ATP} channels are unlikely to involved in the effects of diazoxide and sulphonylureas on mitochondrial function in the beta cell. By contrast, closure of vesicular K_{ATP} channels and enhanced accumulation of Ca^{2+} by these organelles may represent a novel mechanism involved in glucose-stimulated insulin secretion.