

P061 PKC ϵ dependant regulation of Insulin Secretion
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Chronic treatment of pancreatic islets with the lipid palmitate induces defects in glucose stimulated insulin secretion (GSIS) akin to those seen in the development of type II diabetes. Previous studies from our group have identified the lipid-activated kinase protein kinase C epsilon (PKC ϵ) as a potential mediator of some of these effects.

PKC ϵ null mice fed a high-fat diet are protected from diet induced glucose intolerance due to an enhanced responsiveness of the islets to glucose. Islets from these mice display an enhanced 1st and 2nd phase glucose stimulated insulin secretion (GSIS) only in the presence of lipid. Alterations in lipid metabolism suggested an augmentation of the amplification pathway of GSIS in PKC ϵ null mice.

In this study we investigated a number of potential targets of the amplification pathway. Glucose stimulated calcium influx was unaltered by either lipid pre-treatment or PKC ϵ deletion suggesting that PKC ϵ acts at a site distal to calcium influx to inhibit insulin secretion. Analysis of the predocked pool of vesicles in palmitate pretreated β -cells suggests that this is enhanced in PKC ϵ null β -cells. This implicates PKC ϵ in regulating the size of vesicle pools possibly via alterations in signalling associated with the amplification pathway.