Identification of targeted insulin secretion in pancreatic beta cells: evidence for an endocrine synapse

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Spatial targeting of secretion is found in many cell types, most notably in neurones, but is debated for insulin secretion from pancreatic β cells. In this study we have tested this idea using new methods that enable us to image insulin granule fusion from β cells within intact islets.

Experiments were conducted using mouse pancreatic islets. Mice were humanely killed according to local, University of Queensland, animal ethics procedures (approved by the University of Queensland, Anatomical Biosciences Ethics Committee) and the pancreas digested with collagenase. Isolated islets were then incubated overnight to recover.

In live-cell 2-photon imaging of intact islets we demonstrate an asymmetric, non-random, distribution of sites of insulin granule fusion in response to a glucose stimulus. Imaging across two, or more, Z planes we have directly demonstrated focal targeting of insulin granule secretion to the β cell membrane that faces the vasculature. We conclude that the fusion of insulin granules in β cells is spatially targeted.

Next, we set out to determine the potential structural mechanisms within the β cell that might support this targeting. Three-dimensional immunofluorescence of islets shows that structural proteins, associated with neuronal presynaptic targeting, are also found in β cells and are enriched in the region that faces the vasculature. In particular the proteins ELKS and liprin show a strong enrichment along the vascular face.

Our results prove that β cells *in situ*, within intact islets, are polarised and target insulin secretion. We suggest this as evidence for an endocrine synapse with wide implications for our understanding of stimulus-secretion coupling in healthy islets and in disease.