Cell polarity defines three distinct domains in pancreatic beta cells and is disrupted in type 2 diabetes

W.J. Gan,[1] M. Zavortink,[1] A. Shewan[2] and P. Thorn,[1] [1]School of Biomedical Science, University of Queensland, QLD 4072, Australia, and [2]School of Chemistry and Molecular Biosciences, University of Queensland, QLD 4072, Australia..

Loss of insulin secretion is a recognised characteristic of type 2 diabetes. It is therefore an important goal to determine how insulin secretion is controlled and what goes wrong in disease.

Our lab has shown that insulin secretion in pancreatic beta cells is targeted towards the vasculature and that synaptic scaffold proteins, such as liprin, are present in beta cells and enriched at the vascular face of the cells (Low *et al.*, 2014). This demonstrates that beta cells are consistently orientated with respect to the vasculature and implies that cell polarity might be important for proper beta cell function. We therefore aim to study the cell polarity in pancreatic beta cells and its changes in type 2 diabetes.

Immunofluorescent staining of fixed pancreatic slices was used to determine the location of known determinants of cell polarity. Apical determinants, such as Par3, are enriched on the beta cell membrane opposite to the vasculature. Electron microscopy imaging further reveals the detail of apical domain such as the location of primary cilia. In contrast, basal determinants, such as Scribble, are located on the lateral and vascular face of beta cells. To reveal changes of polarity in disease state, we investigate polarity in beta cells of Lerpdb (db/db) mice, an animal model of type 2 diabetes. Our results show that expression of polarity proteins are altered in the diabetic mice as compared to the wild-type mice. Activation of AMP-activated kinase (AMPK), which is important for generating cell polarity, is also reduced in the diabetic mice.

We conclude that beta cells are polarized and have a consistent orientation with respect to the vasculature. Our current data imply that cell polarity may be important to maintain proper beta cell function.

Low JT, Zavortink M, Mitchell JM, Gan WJ, Do OH, Schwiening CJ, Gaisano HY, Thorn P. (2014). Insulin secretion from beta cells in intact mouse islets is targeted towards the vasculature. *Diabetologia* **57**, 1655-1663.