Islet β cell dysfunction in type 2 diabetes – can we save the β cell?

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Type 2 diabetes is characterized by insulin resistance and islet β cell dysfunction that together contribute to hyperglycaemia. However, it is important to highlight that without a defect in islet function resulting in reduced insulin secretion, diabetes does not ensue. There are a number of mechanisms that can contribute to islet β cell dysfunction. Understanding these will provide better therapeutic strategies in treating this disease. We have been working on the hypothesis that overworking the islet β cell is deleterious to its long-term function and survival. To support this hypothesis we have generated a transgenic mouse in which we have slowed metabolism in the islet β cell and show that these mice are protected from high fat induced derangements in glucose tolerance. In addition, large clinical trials including ADOPT and RECORD as well as mutations that lead to Persistent Hypoglycaemia-Hyperinsulinaemia of Infancy (PHHI) support the notion that an overworked β cell may eventually fail. This has management implications as one of the classes of drugs commonly used to treat diabetes stimulate the islet β cell to overwork. We have, therefore, suggested that “metabolic deceleration” is a reasonable strategy to protect the islet beta cell from destruction under conditions of excess nutrient exposure. Thus, approaches that reduce the work-load on the islet β cell must be considered in the long-term treatment of Type 2 diabetes.