**Title:**

Investigating the role of Synaptophysin in beta-cells

**Abstract:**

Background: Healthy insulin secretion from beta-cells is required for the maintenance of blood glucose levels. Glucose-stimulated insulin secretion occurs in two phases: a rapid first phase and a slower second phase. Loss of first phase insulin secretion predicts type 2 diabetes progression at every stage of the disease. Unique populations of insulin granules – as defined by their protein composition and membrane interactions – differentially contribute to first and second phase secretion. Using insulin granule proteomics, our group has recently discovered a novel insulin granule protein – synaptophysin.

Aim: Identify if the protein synaptophysin regulates glucose stimulated insulin secretion in beta-cells

Methods:Western blotting and immunofluorescent co-staining used to evaluate synaptophysin expression in MIN6 beta-cells and human islets. Synaptophysin knockdown achieved using silencing RNA in INS1 rat beta-cells, with insulin content and glucose-stimulated insulin secretion measured 48 hours post-knockdown.

Results: Synaptophysin expression is colocalised with insulin and SNARE protein VAMP2, a marker of pre-docked insulin granules at the beta-cell membrane. Successful knockdown of synaptophysin was observed with ~30% protein expression compared to non-targeting controls. Glucose-stimulated insulin secretion performed 48 hours after synaptophysin knockdown demonstrated significantly impaired glucose-stimulated insulin secretion at 10 min and at 60 min.

Conclusion: Synaptophysin is required for optimal glucose stimulated insulin secretion. It potentially plays a role specifically on pre-docked granules, which contribute primarily to first-phase insulin secretion.