

**P062** Investigation of lipid accumulation induced changes in pancreatic beta-cells using proteomic approaches  
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Type 2 diabetes is a disease characterised by insulin resistance. Strong associations have been made between obesity and the development of the disease. Hyperglycaemia and hyperlipidaemia, are known to cause  $\beta$ -cell dysfunction and exhaustion, but the exact mechanisms involved remain unclear. It is the aim of this study to identify the methods by which glucolipotoxicity affects cellular function.

MIN6 cells, incubated with 0.25mM palmitate and 0.25mM oleic acid (NEFA), in the presence of stimulating (25mM) and non-stimulating (3mM) glucose concentrations, were used as a model of glucolipotoxicity. Accumulation of NEFA in the cells was imaged using Oil Red O and BODIPY®493/503. Cell death was assessed using FACS. The morphology of fixed lipotoxic cells were examined using Transmission Electron Microscopy (TEM). Cell lysates were run on 2D-PAGE with DIGE to identify the differential expression of proteins in lipotoxic and control conditions.

A glucose dependent accumulation of lipid droplets was observed in the cytoplasm of lipotoxic cells (average 8 droplets/ cell in high glucose vs. 1 droplet/ cell in low glucose). Cell viability was not significantly altered (16% control vs. 22% lipotoxic). Distorted ER and large lipid droplets were observed in cells using TEM. 2D-PAGE analysis was carried out on lipotoxic cell lysates and some mitochondrial and cytoskeletal proteins appear to be differentially expressed.

A better understanding of the downstream targets of lipotoxicity are likely to contribute to the development of novel, therapeutic approaches for Type 2 diabetes.