**Introduction**

In the initial stages of type 2 diabetes, people are incapable of producing enough insulin to maintain normal glucose levels as they become insulin resistant. The ability to produce insulin is determined by the total beta cell number, as well as the functional ability of the beta cells. B-cells are adaptable by hyperplasia and neogenesis, but expansion of beta cells is limited by apoptosis. The activation of apoptosis, plus low beta cell division/growth can lead to type 2 diabetes. Glucose can stimulate beta cell growth, but consistently high blood glucose can lead to glucotoxicity and loss of beta cell mass, in genetically susceptible subjects.

Aside from elevated blood glucose levels, blood free fatty acids are also often increased in insulin resistance, which further impedes beta cell function. In certain models, free fatty acids in the blood stream induce beta cell apoptosis. However, these studies were only done in rats with a high fatty acid concentration added to isolated beta cells.

The mechanism is thought to be because of fatty acids being converted to ceramides, which can accumulate and cause apoptosis. Ceramides act as intracellular messengers that can promote cell growth to (in higher concentrations) cell death and cell diminution. Blocking ceramides via drug route (fumonisin B1) shows reduced ceramide production and stopping apoptosis.

For this apoptosis to occur, mitochondrial membranes need to open to allow the outpouring of cytochrome c into the cytosol. This process is controlled by the permeability transition pore - which is a complex of proteins including the abundant protein - adenine nucleotide translocator (ANT). Other proteins like Bax and Bak interact with ANT to induce mitochondrial swelling. Palmitoyl-CoA (a product of palmitate + CoA synthesized by the enzyme Palmitoyl CoA Synthetase) can easily bind ANT - however, if these molecules actually lead to mitochondrial swelling and cytochrome c release is unknown.

**Study Design**

Researchers removed pancreas from anaesthetized rats and then digested to remove non-interest tissues (like structural proteins). After digesting the pancreas, they separated out the pancreatic cells and put them on cell culture plates. From there, they let them attach to the bottom of the plate and ran experiments on these pancreatic cells.

They fed the pancreatic cells a variety of nutrition conditions:

1. 5.5mM Glucose media. (99mg/dL)
2. 11.1mM Glucose media. (200mg/dL)
3. 33.3mM Glucose media. (600mg/dL)

Plus or minus:

1. 0.5mM Palmitate (Saturated Fat)
2. 0.5mM Palmitoleate (Unsaturated Fat)
3. Mixture of both fats (0.25 or 0.5 mM of both).

**Discussion**

The researchers say that this study shows the proliferative ability of beta cells is impaired by palmitate, as well as palmitate causing cell death. On the other hand, palmitoleate, which is identical in the length of the fat molecule leads to an opposite effect - promoting beta cell growth and not causing apoptosis (cell death). Ceramides are required for these negative palmitate effects. Overall, there are improved health parameters from palmitoleate through improved insulin signaling, for example.

Not only that, palmitoleate prevents many of the negative effects seen with palmitate when cells were exposed to both simultaneously. Fat molecules longer than 15 carbons have been shown to be detrimental to some cell types (according to other research). At the same concentrations, other saturated fats also seem to have negative effects mimicking those described here. Interestingly, other monounsaturated fats also displayed the same positive effects on the cells.

The reason offered (hypothetical) is that saturated fats have higher melting points, so triglycerides formed end up precipitating inside organelles like the sarcoplasmic reticulum - reducing its function. Meanwhile, unsaturated fats stay liquid. Another explanation is offered in changes of membrane fluidity - phospholipids enriched with saturated fats lower membrane fluidity and can reduce cell membrane function.

**Amendments**

None.