

P012 Expression of novel lipid regulators in human and rodent islets

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Hormone-sensitive lipase (HSL) has been implicated in the regulation of islet lipid metabolism, insulin secretion and islet function. To gain further insight into the molecular events underlying such regulation we investigated the expression of novel lipid regulators.

In human islets, TaqMan gene expression analysis demonstrated expression of HSL but also of novel enzymes: desnutrin, adiponutrin and triglyceride hydrolase (TGH). In animal disease models, expression of these genes was altered. While expression of desnutrin increased upon fasting in lean C57BL mice there was no change in the obese. In contrast in db/db mice the expression was higher in fasted obese vs. lean mice. Adiponutrin expression was significantly increased in obese db/db mice as well as in obese Zucker rats vs. lean counterparts.

Comparative genomic techniques revealed that rodent TGH1 and TGH2 lie in a cluster of carboxylesterase genes that are orthologous to human TGH. TGH1 expression was significantly downregulated during fasting in lean C57BL mice. The islet expression of TGH2 was found to be upregulated in obese vs. lean Zucker rats, ZDF rats and db/db mice. Finally, broad gene expression profiles for the above-mentioned genes were generated from in house microarray datasets.

This initial study has identified the mRNA expression of novel lipid regulators desnutrin, adiponutrin, TGH1 and TGH2 in pancreatic islets of different species. The functional significance of these findings is so far to be determined.