

P016 TLR agonist induced changes BRIN-BD11 clonal beta cell metabolism, signal transduction and insulin secretion

A Kiely, P Newsholme

*UCD School of Biomolecular and Biomedical Science,
UCD Conway Institute, University College Dublin, Ireland*

Insulin resistance associated with obesity and Type II diabetes is commonly associated with changes in muscle, adipose tissue and liver signal transduction pathways. Pro-inflammatory cytokines (such as TNF- α and IL-1 β) can alter patterns of insulin signalling in these target tissues, resulting in resistance to the action of insulin. More recently evidence for involvement of innate immune product receptors, e.g. Toll like receptors, in insulin resistance has been published. TLR4 and TLR2, whose agonists include lipopolysaccharides and saturated fatty acids, are implicated in altered patterns of signalling in animal models of insulin resistance and obesity. Indeed loss of function mutations in the TLR4 receptor had a beneficial effect on the insulin signalling pathways in adipose, muscle and liver tissues in mice and improved insulin action.

TLR receptor expression has been reported in primary beta cells and some beta cell lines. We have detected the expression of the majority of the TLRs in the BRIN-BD11 pancreatic beta-cell line, including TLR4 and TLR2. We have also recently demonstrated small but significant changes in metabolism and insulin secretion associated with chronic exposure to many of the TLR agonists. With respect to beta cell insulin signalling pathways we have additionally investigated TLR agonist induced changes in signal transduction and have attempted to correlate these alterations with our recent work on TLR agonist induced metabolic and secretory changes.