

P007 Evidence against the involvement of the PI-3 kinase pathway in the cytoprotective actions of monounsaturated fatty acids in pancreatic β -cells

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Introduction: Certain long-chain monounsaturated fatty acids have been shown to attenuate the cytotoxicity associated with treatment of β -cells with saturated fatty acids and serum withdrawal. In some studies, the anti-apoptotic survival pathway involving activation of PI-3-Kinase and Akt has been implicated in this response. However, this has not been observed universally and we have further investigated the role of this pathway in mediating the well-characterised protective actions of palmitoleate (C16:1) in clonal β -cells.

Results and conclusion: Palmitoleate provided complete protection against the cytotoxicity resulting from incubation of clonal β -cells with either palmitate (C16:0) or serum deprivation. This response was not altered by either of the PI-3 Kinase inhibitors wortmannin or LY294002. Moreover, palmitoleate did not cause increased phosphorylation of Akt (a downstream target protein of PI-3 kinase) in β -cells although it did abolish the increase in caspase 3/7 activity mediated by palmitate. By contrast, IGF-1 rapidly and dramatically increased Akt phosphorylation but it failed to attenuate either palmitate-induced caspase3/7 activity or cytotoxicity. We conclude that activation of the PI-3-kinase pathway is not sufficient to prevent palmitate-induced cytotoxicity in β -cells and that this pathway is not involved in mediating the cytoprotective actions of Palmitoleate.