

P040 Inhibition of AMP-activated protein kinase protects pancreatic β -cells from cytokine-mediated apoptosis and CD8+ T cell-induced cytotoxicity.

**Audrey Riboulet-Chavey¹, Frédérique Diraison^{1,2},
L. Khai Siew², F. Susan Wong² and Guy A. Rutter¹**

¹ Imperial College, London, UK; ² University of Bristol, UK

Aims: Apoptotic destruction of pancreatic β -cells is involved in the aetiology of both type 1 and type 2 diabetes. AMP-activated protein kinase (AMPK) is a cellular energy sensor whose sustained activation is implicated in β -cell apoptosis and in islet cell death post-transplantation. Here, we examine the importance of β -cell AMPK in cytokine-induced apoptosis and in the cytotoxic action of CD8+ T-cells. **Methods:** Clonal MIN6 β -cells or CD1 mouse pancreatic islets were infected with recombinant adenoviruses encoding eGFP (Null), constitutively-active AMPK (AMPK CA), or dominant-negative AMPK (AMPK DN) and exposed or not to TNF α , IL-1 β and IFN γ . Apoptosis was monitored through the cleavage of caspase-3 and DNA fragmentation. The cytotoxic effect of CD8+ purified T cells was examined against pancreatic islets from NOD mice infected with either Null or the AMPK DN-expressing adenoviruses. **Results:** Exposure to cytokines or expression of AMPK CA induced apoptosis in clonal MIN6 β -cells and CD1 mouse pancreatic islets. By contrast, inhibition of AMPK protected the β -cells from cytokine-induced apoptosis or the cytotoxic effect of CD8+ T cells. **Conclusion:** Inhibition of AMPK activity enhances islet survival and may therefore represent an interesting therapeutic target to suppress β -cell death.