

P018 Expression and function of cannabinoid receptors by mouse β -cells

Chen Li, James Bowe, Peter Jones, Shanta Persaud
King's College London

Cannabinoid receptors have been identified in a variety of cell types and their activation may be coupled to increases in $[Ca^{2+}]_i$. Given the importance of Ca^{2+} in the regulation of insulin secretion we have examined whether pancreatic β -cells express CB receptors and whether these receptors are functionally coupled. CB1 and CB2 receptors were identified in MIN6 β -cells and mouse islets by RT-PCR and western blotting. Activation of CB1 (10 μ M ACEA) and CB2 (10 μ M JWH015) receptors stimulated increases in $[Ca^{2+}]_i$ in MIN6 cells (peak stimulation: 80 \pm 2% and 104 \pm 4% of 100 μ M ATP response respectively, mean \pm SEM, n=15) and dispersed mouse islet cells (peak stimulation: 102 \pm 3% and 94 \pm 2% of 100 μ M ATP response respectively, n=7). The stimulatory effect of ACEA on $[Ca^{2+}]_i$ was completely inhibited by the CB1 receptor antagonist AM251, to 99 \pm 1% of the basal level). The elevations in $[Ca^{2+}]_i$ were associated with increased insulin secretion at 2mM glucose from both MIN6 pseudoislets (peak stimulation, 10 μ M ACEA: 498 \pm 86%; 10 μ M JWH015: 360 \pm 56%, mean \pm SEM, n=4, P \leq 0.01) and isolated mouse islets (peak stimulation, 10 μ M ACEA: 1195 \pm 48%; 10 μ M JWH015: 722 \pm 37 mean \pm SEM, n=4, P<0.001). Both receptor agonists also potentiated 20mM glucose-stimulated insulin secretion. These data indicate that CB1 and CB2 receptors are expressed by mouse β -cells and that they are coupled to both increased $[Ca^{2+}]_i$ and insulin secretion.