

P001 NAADP-sensitive Ca^{2+} stores contribute to glucose-induced $[\text{Ca}^{2+}]_i$ changes in mouse pancreatic β -cells
Abdelilah Arredouani; Antony Galione
Pharmacology Department, Oxford, UK

In response to its main physiological stimulus glucose, the pancreatic β -cells display $[\text{Ca}^{2+}]_i$ oscillations involving both Ca^{2+} influx and Ca^{2+} release from internal Ca^{2+} stores. We investigated the possible role of NAADP-evoked Ca^{2+} release in glucose-induced β -cell Ca^{2+} signalling. Recent reports suggest that NAADP releases Ca^{2+} from acidic stores. Acute application of Bafilomycin A1 (3 μM), a specific V- H^+ -type ATPase inhibitor, abolishes glucose-induced Ca^{2+} oscillations in β -cells. Pre-treatment of β -cells with bafilomycin completely prevents the $[\text{Ca}^{2+}]_i$ rise in response to an increase of glucose concentration from 3 to 10 or 15 mM. This effect is not due to inhibition of VDCC as demonstrated by the lack of a significant effect on potassium-induced $[\text{Ca}^{2+}]_i$ transients or directly on whole cell Ca^{2+} currents. Moreover, bafilomycin does not increase the K-ATP current in the presence of 10 mM glucose. On the other hand, Bafilomycin increases basal $[\text{Ca}^{2+}]_i$ levels when applied in the absence of extracellular Ca^{2+} suggesting that bafilomycin-sensitive stores do buffer $[\text{Ca}^{2+}]_i$. We also show that low concentrations of NAADP trigger ionic currents when infused through a patch pipette. These currents are inhibited by high NAADP concentrations. All together, our results suggest that the NAADP-induced Ca^{2+} release is likely to have a role in glucose-induced $[\text{Ca}^{2+}]_i$ changes in primary mouse pancreatic β -cell.