GLUCOSE EVOKED REGULATION OF Na,K-ATPASE ACTIVITY IN PANCREATIC β-CELLS

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Glucose is the most important physiological insulin secretagogue. However, the mechanism of glucose-induced insulin release is not fully understood. The current dogma states that, in pancreatic β-cell, glucose metabolism leads to an increase of ATP/ADP ratio, closure of ATP-sensitive K^+ channels, membrane depolarization, opening of the voltage-dependent Ca^{2+} channels and Ca^{2+} influx which triggers insulin exocytosis. However, the role of other electrogenic systems, namely ionic pumps, to these events remains essentially uninvestigated.

Na,K-ATPase, responsible for maintaining Na^+ and K^+ gradients across the plasma membrane, extrudes $3Na^+$ in exchange for $2K^+$, generating a net outward current; Thus changes in its activity may contribute to the ionic events regulating insulin secretion. Regulation of Na,K-ATPase activity by glucose remains unclear and controversial, and has never been determined in intact β-cells.

The aim of this work was to develop a method to characterize Na,K-ATPase activity in intact β-cells and to evaluate whether glucose contributes to its regulation.

Na,K-ATPase activity was determined in both islet homogenates and intact isolated β-cells. Isolated islets were incubated (1h) with different glucose concentrations (2-8.4mM). Subsequently, islets homogenates were prepared and Na,K-ATPase activity was determined. Intact β-cells were isolated and maintained in adherent culture (48h). Cell batches were incubated in 0-11mM glucose (1h). Afterwards, incubation media were substituted by Na,K-ATPase activity determination media. The cells were viable throughout the experiment. Glucose induced a dose-dependent reduction of Na,K-ATPase activity in both islets homogenates and intact β-cells.

In conclusion, this work demonstrates for the first time a regulation of Na,K-ATPase activity by glucose in intact β-cells. Therefore, its contribution to glucose-induced ionic events and insulin secretion might be relevant. We proceed to clarify this hypothesis.

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