THE ROLE OF THE SODIUM-CALCIUM EXCHANGER IN REGULATING CYTOSOLIC CALCIUM CONCENTRATION IN RAT PANCREATIC B CELLS

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1. The present study was carried out to clarify the role of the Na^+/Ca^{2+} exchanger in regulating the cytosolic Ca^{2+} concentration ($[Ca^{2+}]_c$) in rat pancreatic B cells. To analyze the characteristics of the exchanger, influences of extracellular Na^+ concentration ($[Na^{2+}]_0$) and various inhibitors on $[Ca^{2+}]_c$ were examined by a microfluorometric method using Fura-2 in isolated perifused preparations of rat pancreatic islets.

2. Removal of extracellular Na^+ ($Na^+{}_0$) caused an abrupt increase in $[Ca^{2+}]_c$ and partial removal of $Na^+{}_0$ resulted in respective rises in $[Ca^{2+}]_c$ in relation to level of reduced $[Na^+]_0$. A quantitative relation was found between $[Ca^{2+}]_c$ and $[Na^+]_0$ over the range 0–146mM. The relation fitted the Hill equation, the coefficient of which was 2.6.

3. Removal of $CaCl_2$ from the perifusion solution produced a definite inhibition in the $[Ca^{2+}]_c$ rise induced by the $Na^+{}_0$ removal, and reintroduction of Ca^{2+} to the Na^+-deficient environment caused an abrupt increase in $[Ca^{2+}]_c$.

4. The rise in $[Ca^{2+}]_c$ induced by the $Na^+{}_0$ removal was inhibited dose-dependently by Ni^{2+}, which is known to be a competitive inhibitor of Ca^{2+} influx in various types of secretory cells.

5. In contrast, nifedipine (10 μM), which is known to inhibit voltage-dependent L-type Ca^{2+} channels, had little, if any, effect on the $[Ca^{2+}]_c$ rise induced by the $Na^+{}_0$ removal.

6. Ouabain (2mM), which is known to inhibit the Na^+-K^+ ATPase, enhanced the $[Ca^{2+}]_c$ rise induced by the $Na^+{}_0$ removal.

7. These results are compatible with the view that the $[Ca^{2+}]_c$ rise induced by the $Na^+{}_0$ removal is due to an increase in Ca^{2+} influx mediated by the Na^+/Ca^{2+} exchanger. This view is supported by the following results; (1) the $[Ca^{2+}]_c$ rise induced by the $Na^+{}_0$ removal can be ascribed to a Ca^{2+} influx, (2) the Ca^{2+} influx is not mediated by voltage-dependent L-type Ca^{2+} channels, (3) the $[Ca^{2+}]_c$ rise depends on the transmembrane Na^+ gradient, and (4) the quantitative relation between $[Na^+]_0$ and $[Ca^{2+}]_c$ fits the Hill equation, the coefficient of which was about 3. It is thus concluded that the Na^+/Ca^{2+} exchanger plays a cardinal role in the mechanism regulating $[Ca^{2+}]_c$ in rat pancreatic B cells.