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タイトル
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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\(^+\)]\(_0\)) and various inhibitors on [Ca\(^{2+}\)]\(_c\) were examined by a microfluorometric method using Fura-2 in isolated perfused 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\(^+\) 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 0–146 mM. 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\(^+\) 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\(^+\) 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 \(\mu\)M), 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\(^+\) removal.

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

7. These results are compatible with the view that the [Ca\(^{2+}\)]\(_c\) rise induced by the Na\(^+\) 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\(^+\) 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.