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+/Ca2+ exchanger in regulating the cytosolic Ca2+ concentration ([Ca2+]c) in rat pancreatic B cells. To analyze the characteristics of the exchanger, influences of extracellular Na+ concentration ([Na+0]) and various inhibitors on [Ca2+]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 [Ca2+]c and partial removal of Na+0 resulted in respective rises in [Ca2+]c in relation to level of reduced [Na+0]. A quantitative relation was found between [Ca2+]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 CaCl2 from the perifusion solution produced a definite inhibition in the [Ca2+]c rise induced by the Na+0 removal, and reintroduction of Ca2+ to the Na+-deficient environment caused an abrupt increase in [Ca2+]c.

4. The rise in [Ca2+]c induced by the Na+0 removal was inhibited dose-dependently by Ni2+, which is known to be a competitive inhibitor of Ca2+ influx in various types of secretory cells.

5. In contrast, nifedipine (10μM), which is known to inhibit voltage-dependent L-type Ca2+ channels, had little, if any, effect on the [Ca2+]c rise induced by the Na+0 removal.

6. Ouabain (2mM), which is known to inhibit the Na+–K+ ATPase, enhanced the [Ca2+]c rise induced by the Na+0 removal.

7. These results are compatible with the view that the [Ca2+]c rise induced by the Na+0 removal is due to an increase in Ca2+ influx mediated by the Na+/Ca2+ exchanger. This view is supported by the following results; (1) the [Ca2+]c rise induced by the Na+0 removal can be ascribed to a Ca2+ influx, (2) the Ca2+ influx is not mediated by voltage-dependent L-type Ca2+ channels, (3) the [Ca2+]c rise depends on the transmembrane Na+ gradient, and (4) the quantitative relation between [Na+0] and [Ca2+]c fits the Hill equation, the coefficient of which was about 3. It is thus concluded that the Na+/Ca2+ exchanger plays a cardinal role in the mechanism regulating [Ca2+]c in rat pancreatic B cells.