CORRELATION BETWEEN STIMULUS-SECRETION COUPLING AND FUROSEMIDE-SENSITIVE ION TRANSPORT IN RAT PANCREATIC ACINI

—— An approach monitoring digestive enzyme release and concentration of intracellular calcium ions ——

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1. The present study was carried out to examine the relationship between stimulus-secretion coupling and ion transport. The cytosolic concentration of calcium ion ($[Ca^{2+}]_c$) of isolated pancreatic acini from the rat loaded with fura-2 was monitored by microspectrofluorometry. Under comparable experimental conditions, acini loaded with fura-2 were perifused with modified Krebs-Henseleit bicarbonate-buffered solution and amylase release from the perifused acini was monitored.

2. During continuous stimulation with 10pM CCK-8, amylase released from acini increased rapidly to reach a plateau level three times greater than the resting level. Cessation of the stimulation resulted in a gradual decrease in amylase release, reaching the resting level within about 15 min. Stimulation with CCK-8 induced a sustained increase in $[Ca^{2+}]_c$ with oscillatory change. During perifusion with Ca^{2+}-free solution with 1mM EGTA, amylase release induced by 10pM CCK-8 was strongly inhibited but a small and transient increase remained in the initial phase of the secretory response. The sustained increase in $[Ca^{2+}]_c$ was abolished but the oscillation remained in the $[Ca^{2+}]_c$-free environment.

3. Furosemide (1mM) reduced amylase release induced by 10pM CCK-8 to the resting level. Administration of 1mM furosemide alone decreased transiently the resting level of amylase release. Furosemide (1mM) abolished the sustained increase in $[Ca^{2+}]_c$ induced by 10pM CCK-8 and decreased oscillatory amplitude and frequency.

4. The CCK-8-induced secretory response was unchanged by perifusion with a solution containing 0.1mM ouabain, and with a K^+-free or Na^+-deficient solution to inhibit Na^+, K^+-ATPase activity. The response was also uninfluenced by administration of 1mM amiloride or 0.1mM SITS. Replacement of Cl^- with isethionate inhibited amylase release induced by 10pM CCK-8.

5. On the basis of the present results, the following mechanism is proposed: Binding of CCK-8 to CCK-receptors in the membrane of pancreatic acinar cells may cause an influx of extracellular Ca^{2+} and, in turn, the increase in $[Ca^{2+}]_c$ may induce exocytosis of zymogen granules.