A-19 Identification of mini-glucagon receptor(s) from rat hepatocytes

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Mini-glucagon (glucagon-(19-29)), which is derived by proteolytic cleavage of native glucagon, inhibits the Ca^{2+} pump in liver plasma membranes, with concomitant inhibition of the high affinity (Ca^{2+} - Mg^{2+}) - ATPase activity. The regulation of the liver plasma membrane Ca^{2+} pump by mini-glucagon is independent of adenylate cyclase activation by glucagon. Therefore, in recent years, evidence for the existence of a receptor for mini-glucagon has increasingly been accumulated. The identification of such a recognition site will facilitate the understanding of complex processes associated with the inhibition of the Ca^{2+} pump by mini-glucagon.

The present study was designed to determine whether there are 2 different receptors for glucagon and mini-glucagon with the objective of isolation and characterization of mini-glucagon receptor(s).

Highly purified rat liver plasma membrane vesicles were prepared by centrifugation in a percoll self forming gradient. ATP-dependent Ca^{2+} uptake, (Ca^{2+} - Mg^{2+})-ATPase activity and adenylate cyclase activity were measured in inside-out plasma membrane vesicles in reaction mixtures containing varying concentrations of glucagon and mini-glucagon in the presence of bacitracin, an inhibitor of glucagon degradation.

A constant inhibition of Ca^{2+} - pump and (Ca^{2+} - Mg^{2+})-ATPase activity, together with an increased adenylate cyclase activity were observed when mini-glucagon concentration remained constant and concentration of glucagon was increased. Moreover an increased inhibition of Ca^{2+} - pump and (Ca^{2+} - Mg^{2+})-ATPase activity, together with a constant adenylate cyclase activity were observed in response to a constant glucagon concentration and an increased mini-glucagon concentration.

These results show exclusivity of the specific receptor/ligand interactions, namely glucagon receptor / glucagon and mini-glucagon receptor / mini-glucagon and therefore, the existence of 2 different very specific receptors for the 2 ligands without any cross reactivity.

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