Characterization of Mini-Glucagon receptors from Rat Hepatocytes

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Manamperi, Assalarachchige Aresha Priyanka Samarasinghe

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Abstract:

Nanomolar concentrations of glucagon - (19-29) (referred to as mini glucagon)which is derived by proteolytic cleavage of the dibasic doublet Arg17 - Arg18 of native glucagon, inhibit the Ca2+ pump in liver plasma membranes, with a concomitant inhibition of the high affinity (Ca2+ - Mg2+)-ATPase activity. However this biphasic regulation of the liver plasma membrane Ca2+ pump by glucagon - (19 - 29) is independent of adenylate cyclase activation by glucagon. A considerable body of evidence also suggests that a cholera toxin-sensitive protein, perhaps a Gs or a Gs-like protein is involved in this biphasic regulation of Ca2+ pump by glucagon-(19-29). In recent years, evidence for the existence of a recognition site for glucagon-(19-29) has increasingly been accumulated. The identification of such a recognition site will be of great importance since it will facilitate the understanding of complex processes associated with the inhibition of the Ca2+ pump by glucagon-(19-29). The present
study was designed to ascertain whether liver plasma membranes have two different receptors for glucagon and glucagon-(19-29), with the objective of isolation and characterization of glucagon -(19-29) receptor(s). In these experiments, adenylate cyclase activity, (Ca2+-Mg2+)-ATPase activity and ATP-dependent Ca2+ uptake inhibition were assayed independently under identical conditions, in reaction mixtures containing varying concentrations of glucagon and glucagon-(19-29) using rat liver plasma membrane vesicles isolated by the Percoll self forming gradient centrifugation in isotonic medium. Results of this study showed the presence of specific receptor/ligand nteractions for glucagon and glucagon-(19-29) and provided the first line experimental evidence for the existence of two different very specific receptors for glucagon and glucagon-(19-29) and also for the absence of any cross reactivities between the two receptor/ligand pairs.

Key Words : Receptors, Glucagon-chemistry/Receptors, Glucagon-genetics/Receptors, Glucagon-metabolism/Rats