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Reviews

Stimulus-secretion coupling in the pancreatic B-cell

Coordinator: W.J. Malaisse, Brussels

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Stimulus-secretion coupling in the pancreatic B-cell: introductory remarks

by W.J. Malaisse

Laboratory of Experimental Medicine, Brussels Free University, B–1000 Brussels (Belgium)

Key words. Pancreatic B-cell; stimulus-secretion coupling.

Insulin plays a key role in fuel homeostasis in man and other species. Hence, a deficient or excessive secretion of insulin results in severe metabolic disturbances such as those encountered in diabetes mellitus or certain hypoglycemic syndromes. The regulation of insulin release in vivo therefore represents a topic of obvious interest. Such a regulation seems to be placed under the control of two series of factors. The first factors exert an immediate and direct effect upon insulin release by the pancreatic B-cell. They include circulating nutrients, hormones and neurotransmitters. The second factors influence the secretory behavior of the B-cell in a delayed fashion. They include ontogenic, nutritional and endocrine factors. Any attempt to understand how these several factors interact to provide an adequate supply of insulin to extrapancreatic tissues depends on our knowledge on the functional organization of endocrine cells in the islets of Langerhans. The presents series of reports deals essentially with such a cytophysiology of insulin release.

The secretory response of the pancreatic B-cell to a change in its environment, e.g. an increase in the extra-

cellular concentration of glucose, appears to be mediated by a coordinated set of cellular events. These include the perception of the environmental change, its translation into a coupling mechanism and the eventual modification in the rate of insulin release. Such a sequence of events may be viewed as the process of stimulus-secretion coupling. It is often assumed that, in the B-cell, the information generated by distinct sensor systems is integrated to regulate, in a coordinated manner, a single and terminal process of insulin release, which corresponds to the exocytosis of secretory granules. Thus, distinct regulatory factors may feed in at distinct levels in the secretory sequence.

It is a demanding and occasionally frustrating ambition to provide a cartesian explanation for the cause-to-effect links between distinct, though almost simultaneous, events involved in the process of stimulus-secretion coupling. Indeed, as knowledge progresses in this field and the progress is obvious as judged for instance from successive multi-authors reviews on this topic[1-5], it became evident that almost any cellular process is affected by or participates in stimulus-secretion coupling. For instance, when the extracellular concentration of glucose is increased, changes in the B-cell involve the metabolism of nutrients, the consumption of O_2 and redox state, the heat production, the intracellular pH, the biosynthesis of proteins, the fluxes of several ions, the electrical activity, the turnover of phospholipids, the (de)phosphorylation of proteins, the fluidity of membranes, the production of cyclic AMP, the contractile activity of the cell web, the movements of secretory granules, the coupling of endocytosis to exocytosis and the intercellular communication between adjacent cells. Which of these changes occurs first, and how are they interconnected? It is the very aim of this series of reports to answer such questions. Each contributor to this review would probably accept the blame that it presently looks as an impossible dream to reach an unambiguous answer.

It seems mandatory to underline several restrictions in the scope and content of this review. First, the topic is restricted to the insulin-producing B-cell. The cytophysiology of adjacent non-B endocrine cells in the islets is not discussed. Second, the emphasis is given to the cytophysiology of insulin release. Other aspects of the anatomic and functional organization of the B-cell, e.g. the synthesis and conversion of proinsulin, are only considered as far as they are immediately relevant to the secretory process. Third, this review is conceived from the standpoint of cellular physiology, and not in the perspective of the regulation of insulin release in vivo. Hence, such topic as the neural and hormonal control of insulin release, e.g. by gastrointestinal factors, is not reviewed. Fourth, emphasis is given on the cellular events involved in the rapid process of stimulus-secretion coupling. The long-term regulation of islet function by ontogenic, nutritional and endocrine factors is not dealt with. Last, this review concerns the physiology, and not the pathology, of insulin-producing cells. No information is provided on the anomaly of B-cell function found in experimental or spontaneous diabetic syndromes or tumoral insulin-producing cells. I can only apologize for these restrictions. Needless to say, they do not reflect any lack of interest for the topics omitted from this review, but instead were imposed by considerations on both the homogeneity and length of this contribution. It is nevertheless hoped that potential readers may be interested by the information provided in this review.

1 Brolin, S.E., Hellman, B., and Knutson, H., The structure and metabolism of the pancreatic islets. The Macmillan Company, New York 1964.
2 Cooperstein, S.J., and Watkins, D., The islets of Langerhans. Biochemistry, physiology and pathology. Academic Press, New York 1981.
3 Falkmer, S., Hellman, B., and Täljedal, I.-B., The structure and metabolism of the pancreatic islets. Pergamon Press, Oxford, New York 1970.
4 Hasselblatt, A., and Bruchhausen, F. v., Insulin, part 2, in: Handbook of Experimental Pharmacology. Springer Verlag, Berlin 1975.
5 Malaisse, W.J., and Täljedal, I.-B., Biochemistry and biophysics of the pancreatic B-cell. Horm. Metab. Res., suppl. 10 (1980).
6 Steiner, D.F., and Freinkel, N., Endocrine pancreas, in: Handbook of Physiology, Am. Physiol. Soc. Washington, D.C., 1972.

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Nutrient metabolism in islet cells

by A. Sener and W.J. Malaisse

Laboratory of Experimental Medicine, Brussels Free University, B-1000 Brussels (Belgium)

Key words. Pancreatic B-cell; nutrient metabolism.

1. Introduction

D-glucose and a variety of other nutrients are able, under suitable experimental conditions, to stimulate insulin release from the pancreatic B-cell. For some time, it had been proposed that the stimulant action of these nutrients upon insulin release may be mediated through stereospecific (membrane) receptors, the binding of each nutrient to its specific receptor initiating the sequence of events eventually leading to the exocytosis of