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Direction of insulin to regulatory secretory pathway: Possible role in diabetes mellitus

High blood insulin concentration at basal conditions without appropriate response to glucose stimulation is common symptom in patients with diabetes mellitus 2 considered to be result of insulin resistance. Pancreatic thyrotropin-releasing hormone (TRH) is co-localized with insulin in the secretory granules of β cells. We showed that secretion of TRH from islets is stimulated by glucose and inhibited by insulin or somatostatin. Moreover, it was shown that *prepro*-TRH gene disruption in mice results in hyperglycemia, accompanied by impaired insulin response to glucose stimulation. These data indicate specific relation between TRH and glucose-induced insulin secretion. To induce acute shortage of TRH we blocked the terminal step of the post-translational TRH maturation in adult rat *in vivo* by disulfiram (DS, 5 day i.p. 200 mg/kg pretreatment) and tested insulin secretion from isolated islets *in vitro*. Release of insulin from DS-treated pancreatic islets under basal (unstimulated) conditions was four times higher compared to control and could not be further stimulated by high-glucose. Addition of 1 nM TRH in the incubation medium immediately decreased basal insulin secretion to control levels and normalized response to 16.7 mM glucose of islets from DS treated rats. Apparently, pancreatic TRH is necessary for adequate insulin secretion at basal condition and response to glucose stimulation. We conclude that TRH is essential for insulin direction from constitutional to regulatory secretory pathway. This function might be disturbed in diabetes mellitus 2.

Biography

Vladimír Štrbák has completed his study in Bratislava. He was the Director of Institute of Experimental Endocrinology- SAS, Slovakia, and the Head of Pathological Physiology, Slovak Medical University, Slovakia. He is the President of the Slovak Physiological Society, Council Member FEPS, Chair of the Scientific Board of the Slovak Academy of Sciences for Medical Sciences, and Council Member of the International Society for Pathophysiology. He has 137 published PubMed papers. He has served as an Organizing Committee Member of the Global Diabetes Summit and Medicare Expo in Dubai (2015) and Birmingham (2016).

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