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Thyrotropin releasing hormone and insulin regulatory secretory pathway

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Thyrotropin-releasing hormone (TRH) was initially isolated as thyrotropin regulating hypothalamic peptide. TRH was found also in various locations. Pancreatic TRH is co-localized with insulin in the secretory granules of β cells. High TRH expression in the pancreatic islets in perinatal rat coincides with maturation of the insulin secretory responsiveness to glucose. Prepro-TRH gene disruption in mice results in hyperglycemia, accompanied by impaired insulin response to glucose. Neonatal STZ administration is followed by partial insulin regeneration, and irreversible destruction of TRH system with persistent disturbance of the insulin response to glucose. We showed that secretion of TRH from islets is stimulated by glucose and inhibited by insulin or somatostatin. 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. TRH in physiological concentration (1 nM) did not affect basal or glucose stimulated insulin secretion. Release of insulin from DS-treated pancreatic islets under basal (unstimulated) conditions was four times higher compared to controls and could not be further stimulated by high-glucose. Presence of 1 nM TRH in the incubation medium decreased basal insulin secretion to control levels and normalized response to 16.7 mM glucose of islets from DS treated rats. We conclude that TRH is essential for insulin direction from constitutional to regulatory secretory pathway. Its role in DM 2 is likely.

Biography

Vladimír Štrbák has completed MD study (1966) at Medical School, Comenius University Bratislava, Ph.D. (1974) and DSc. received at Institute of Experimental Endocrinology, Slovak Academy of Sciences. He was Director of the Institute, president of the Slovak Physiological Society, Council Member of the of the Federation of European Physiological Societies and Council Member of the International Society for Pathophysiology, chair of the Scientific Board of the Slovak Academy of Sciences for Medical Sciences.

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