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### Thyrotropin releasing hormone and insulin regulatory secretory pathway

Thyrotropin-releasing hormone (TRH) was initially isolated as thyrotropin regulating hypothalamic peptide, later was found in various locations. Pancreatic TRH is colocalized with insulin in the secretory granules of  $\beta$  cells. We showed that secretion of TRH from islets is stimulated by glucose and inhibited by insulin or somatostatin. High TRH expression in the pancreatic islets in perinatal rat coincides with maturation of the insulin secretory responsiveness 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. Prepro-TRH gene disruption in mice results in hyperglycemia, accompanied by impaired insulin response to glucose. 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. TRH in physiological concentration (1 nM) does not affect basal or glucose stimulated insulin secretion in control. Release of insulin from DS-treated pancreatic islets under basal (unstimulated) conditions is four times higher compared to controls and could not be stimulated by high-glucose. Addition of 1nM TRH to 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. Research of the potential benefit of its application looks promising.

### Biography

Vladimir 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. Published 117 PubMed papers, served as Associate Editor of Cellular and Molecular Neurobiology for Europe and organized series of International symposia.

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