Involvement of PI-PLCβ1 in insulin secretion in MIN6 pancreatic β-cells

Roberta Fiume, Giulia Ramazzotti, Anna Maria Billi, Lucio Cocco, Francesco Antonio Manzoli
Cellular Signalling Laboratory, Department of Anatomical Sciences, University of Bologna, Italy

Diabetes is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs (WHO 1999). Its prevalence worldwide was 171,000,000 in 2000 and it is estimated 366,000,000 in 2030.

Failure of pancreatic β-cells in insulin secretion plays a major pathogenic role in the emergence of type 2 diabetes mellitus. Inositol lipid metabolism is involved in complex signalling pathways that regulate the stimulus-secretion coupling processes.

In particular, evidences indicate that the activation of phosphoinositide-specific phospholipase C (PI-PLC) and the resulting hydrolysis of phosphatidylinositol-4,5-bisphosphate [PtdIns(4,5)P2] in diacylglycerol (DAG) and inositol 1,4,5-trisphosphate [Ins(1,4,5)P3] are critical to several events such as opening of Ca2+ stores, mediating the effect of many hormones and neurotransmitters and regulating gene expression.

We used murine MIN6 pancreatic β-cells to investigate the role of PI-PLCβ1 in insulin secretion.

Analysis of the subcellular distribution revealed that PI-PLCβ1 localized mainly in the nuclei, as observed by immunocytochemical analysis at TEM and by western blot. PI-PLCβ1 is involved in basal insulin secretion, since PI-PLCβ1 silencing, by means of siRNAs, resulted in a decreased level of insulin secretion at low glucose dose. We have performed PCR array profiling to identify signal transduction pathways involved in insulin secretion, regulated by PI-PLCβ1. From these studies many genes resulted up- or down-regulated when PI-PLCβ1 in silenced, and brought to interest on PI-PLCβ1 signal transduction in β-cells.

Key words PI-PLCβ1, inositol signalling, cell metabolism