Complicações diabéticas se correlacionam com a ativação das proteino kinases: Hiperglicemia ativa PKCs

Activation of protein kinase C isoforms and its impact on diabetic complications.

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Source
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Abstract
Both cardio- and microvascular complications adversely affect the life quality of patients with diabetes and have been the leading cause of mortality and morbidity in this population. Cardiovascular pathologies of diabetes have an effect on microvenules, arteries, and myocardium. It is believed that hyperglycemia is one of the most important metabolic factors in the development of both micro- and macrovascular complications in diabetic patients. Several prominent hypotheses exist to explain the adverse effect of hyperglycemia. One of them is the chronic activation by hyperglycemia of protein kinase (PK)C, a family of enzymes that are involved in controlling the function of other proteins. PKC has been associated with vascular alterations such as increases in permeability, contractility, extracellular matrix synthesis, cell growth and apoptosis, angiogenesis, leukocyte adhesion, and cytokine activation and inhibition. These perturbations in vascular cell homeostasis caused by different PKC isoforms (PKC-alpha, -beta1/2, and PKC-delta) are linked to the development of pathologies affecting large vessel (atherosclerosis, cardiomyopathy) and small vessel (retinopathy, nephropathy and neuropathy) complications. Clinical trials using a PKC-beta isoform inhibitor have been conducted, with some positive results for diabetic nonproliferative retinopathy, nephropathy, and endothelial dysfunction. This article reviews present understanding of how PKC isoforms cause vascular dysfunctions and pathologies in diabetes.

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Schematic representation of biological targets of PKC isoform activation and synthesis
Figure 6
Schematic representation of various biological targets of PKC activation leading to diabetic nephropathy
Figure 3
Schematic representation of hyperglycemia-induced PKC activation affecting multiple cellular functions.
Figure 5
Schematic representation of potential biological targets of PKC activation causing diabetic retinopathy.
Figure 4
Schematic representation of various biological targets of PKC activation leading to selective insulin resistance and diabetic cardiomyopathy