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Fibroblast growth factor acts upon the transcription of phospholipase C genes in human umbilical vein endothelial cells

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Abstract Besides the control of calcium levels, the phosphoinositide-specific phospholipases C (PI-PLCs), the main players in the phosphoinositide signalling pathway, contribute to a number of cell activities. The expression of PI-PLCs is strictly tissue specific and evidence suggests that it varies under different conditions, such as tumour progression or cell activation. In previous studies, we obtained a complete panel of expression of PI-PLC isoforms in human umbilical vein endothelial cells (HUVEC), a widely used experimental model for endothelial cells (EC), and demonstrated that the expression of the PLC genes varies under inflammatory stimulation. The fibroblast growth factor (FGF) activates the PI-PLC γ1 isoform. In the present study, PI-PLC expression in FGF-treated HUVEC was performed using RT-PCR, observed 24 h after stimulation. The expression of selected genes after stimulation was perturbed, suggesting that FGF affects gene transcription in PI signalling as a possible mechanism of regulation of its activity upon the AkT-PLC pathway. The most efficient effects of FGF were recorded in the 3–6-h interval. To understand the complex events progressing in EC might provide useful insights for potential therapeutic strategies. The opportunity to manipulate the EC might offer a powerful tool of considerable practical and clinical importance.

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Introduction

The morphology, the molecular expression and the activities of endothelial cells (EC) vary under the influence of the surrounding environment [1–3]. ECs react to different stimuli with finely tuned responses mediated by different signal transduction pathways, thus leading the endothelium to adapt [1].

The fibroblast growth factor (FGF) proteins constitute a large family of growth factors playing important roles in the regulation of a number of events, including angiogenesis [4].

In EC, basic FGF (also known as FGF-2 or FGF-β) acts as an autocrine effector, which induces cell growth, migration, DNA synthesis, plasminogen activation and metalloproteinase production [5]. Binding to fibroblast growth factor receptors [6] initiates several signal transduction cascades, including the phosphoinositide (PI) pathway, which comprises the Phosphoinositide-specific Phospholipase C (PI-PLC) family of enzymes [7, 8].

PI-PLC enzymes regulate the spatio-temporal balance of the PI metabolism [9, 10]. Once activated, PI-PLC cleaves the membrane phosphatidyl inositol 4,5 bisphosphate (PIP2) into inositol trisphosphate (IP3) and diacylglycerol, crucial molecules in the transduction of signals [11–13].

Thirteen mammalian PI-PLC enzymes were identified, divided into six sub-families on the basis of size, amino acid sequence, domain structure and mechanism of recruitment: β(1–4), γ(1–2), δ(1, 3–4), ε(1), ζ(1) and

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