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论著

糖皮质激素诱导的蛋白激酶3种亚型在高糖诱导的人肾小管上皮细胞中的表达

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摘要 目的：研究高糖环境下人近端肾小管上皮细胞（HKC）中血清和糖皮质激素诱导的蛋白激酶（SGK）3种亚型SGK1、SGK2和SGK3的表达，探讨SGK 3种亚型在介导高糖致肾小管上皮细胞过度合成细胞外基质（ECM）中的作用。 方法: 将细胞分为对照组、高糖组和渗透压对照组。分别采用RT-PCR方法和Western blotting方法检测SGK1、SGK2和SGK3 mRNA水平和SGK1蛋白水平的表达，ELISA方法和间接免疫荧光方法检测培养液中和HKC胞内纤连蛋白（FN）含量。 结果: HKC细胞中存在SGK1、SGK2和SGK3的表达。高糖刺激下， SGK1、SGK2和SGK3 mRNA和SGK1蛋白表达明显升高（P<0.01）；同时伴有HKC FN合成和分泌的增加，这与SGK上调存在一定联系。 结论: 高糖能促进近端肾小管上皮细胞SGK1、SGK2和SGK3的表达，并可能通过SGK1、SGK2和SGK3介导的信号转导途径促进细胞外基质积聚，可能在糖尿病肾病的发生和发展中发挥致病作用。

关键词 糖皮质激素类； 蛋白激酶类； 高糖； 肾小管,近端； 纤维蛋白类

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Expression of SGK isoforms in human proximal tubular epithelial cells under the condition of high glucose concentration

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Abstract

<FONT face=Verdana>AIM: To investigate the effect of high glucose concentration on serum and glucocorticoid induced protein kinase (SGK) mRNA and protein expressions in human proximal tubular epithelial cells (HKC) and the possible role of SGK in the production of extracellular matrix (ECM) of HKC under the condition of high glucose. METHODS: HKC was divided into 3 groups: control glucose group (CG group, 5.5 mmol/L D-glucose); high glucose group (HG group, 25 mmol/L D-glucose) and osmotic control group (MG group, 19.5 mmol/L mannitol and 5.5 mmol/L D-glucose). The expressions of SGK mRNA and protein were assessed by semi-quantitative RT-PCR and Western blotting respectively. The level of secretary and cytoplasmic fibronectin (FN) were detected by enzyme-linked immunoabsorbent assay (ELISA) and indirect-immunofluorescence. RESULTS: HKC expressed SGK1, SGK2 and SGK3 at mRNA and protein levels. Their mRNA level were up-regulated since 2 hours after cells exposed to D-glucose and this up-regulation persisted to the end of 8th hour, and SGK1 protein level elevated simultaneously. On the other hand, the increased FN secretion by high glucose was in a time-dependent manner and its improved secretion threshold was just followed by the high expression of SGK1. CONCLUSIONS: In response to high glucose, the expression of SGK1, SGK2 and SGK3 in human proximal tubular epithelial cells were up-regulated which was accompanied with FN accumulation. The high expression of SGK may mediate overproduction of ECM in proximal tubular epithelial cells and contribute to the diabetic nephropathy.</FONT>

Key words Glucocorticoids Protein kinases High glucose Kidney tubules proximal Fibronectins

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