

论文

Exendin-4体外通过抑制NF- $\kappa$ B-iNOS-NO信号减轻氧化应激诱导的小鼠MIN6胰岛 $\beta$ 细胞凋亡

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摘要:

探讨胰高血糖素样肽-1受体激动剂Exendin-4(Ex-4)在氧化损伤诱导胰岛 $\beta$ 细胞凋亡中的保护作用。培养的MIN6胰岛 $\beta$ 细胞,通过AO-EB染色观察细胞凋亡形态,Annexin-V-PI染色流式技术测定凋亡率,Griess法检测细胞内一氧化氮水平,Western blotting检测胞浆iNOS蛋白、胞浆及胞核核因子- $\kappa$ Bp65(NF- $\kappa$ Bp65)蛋白表达水平。Ex-4可抑制叔丁基过氧化氢(*t*-BHP)诱导的 $\beta$ 细胞凋亡,Ex-4(100 nmol·L<sup>-1</sup>)预处理较单独*t*-BHP处理,其凋亡率减少约67%(*P*<0.001)。Ex-4同时减少NO水平的增高,并抑制*t*-BHP诱导的 $\beta$ 细胞NF- $\kappa$ Bp65活化及iNOS蛋白表达水平。Ex-4可能通过抑制细胞内NF- $\kappa$ B活化、胞浆iNOS表达来抑制NO水平,最终减轻氧化损伤诱导的 $\beta$ 细胞凋亡。

关键词: Exendin-4 胰岛 $\beta$ 细胞 细胞凋亡 核因子 $\kappa$ B 诱导型一氧化氮合酶 一氧化氮 叔丁基过氧化氢

Exendin-4 protected murine MIN6 pancreatic  $\beta$ -cells from oxidative stress-induced apoptosis *via* down-regulation of NF- $\kappa$ B-iNOS-NO pathway

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Abstract:

To explore the effect of glucagon-like peptide-1 receptor agonist-Exendin-4 (Ex-4)on murine MIN6 pancreatic  $\beta$ -cells apoptosis induced by oxidative stress, the morphological changes of cell damage were evaluated by epifluorescence microscopy after staining with AO-EB. The percentage of cell apoptosis was determined by flow cytometric assay after Annexin-V-FITC-PI staining. Nitric oxide level was measured by Griess reagent assay. Inducible nitric oxide synthase (iNOS) protein and NF- $\kappa$ Bp65 fragment were detected by Western blotting. Ex-4 inhibited the increase of nitrite level and percentage of apoptosis induced by *t*-BHP in MIN6 cells. Furthermore, Ex-4 partly reduced the expression of iNOS protein and the ratio of NF- $\kappa$ Bp65 protein in nucleus:cytosol induced by *t*-BHP. These results suggest that Ex-4 protects MIN6 pancreatic  $\beta$ -cells from oxidative stress-induced apoptosis *via* down-regulation of NF- $\kappa$ B-iNOS-nitric oxide pathway.

Keywords: pancreatic  $\beta$ -cell apoptosis nuclear factor- $\kappa$ B inducible nitric oxide synthase nitric oxide *tert*-butyl hydroperoxide Exendin-4

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