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论著

辛伐他汀对同型半胱氨酸诱导的HUVEC的毒性和炎症反应的影响及分子机制

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摘要 目的：探讨辛伐他汀对同型半胱氨酸(HCY)诱导的内皮细胞毒性和炎症的抑制作用及其分子机制。 方法：采用MTT检测细胞活性，通过DCFH-DA检测活性氧的生成，Western blotting分析相关蛋白的表达，凝胶滞留法(EMSA)分析NF-κB的DNA结合活性。 结果： HCY处理后，MTT检测发现内皮细胞存活率显著低于对照，流式细胞仪的结果表明活性氧的水平也显著升高。经不同浓度的辛伐他汀预处理后，可以显著地抑制HCY诱导的内皮细胞存活率的下降以及活性氧水平的升高。Western blotting与ELISA结果发现辛伐他汀抑制TNF-α、IL-6、MCP-1及ICAM-1的表达水平。EMSA和Western blotting检测结果表明辛伐他汀抑制HCY介导的p38磷酸化水平以及通过抑制IκBα磷酸化而抑制IκBα蛋白的降解，阻断HCY诱导NF-κB的激活。 结论： 辛伐他汀对HCY介导的内皮细胞毒性及炎症反应有明显的抑制作用，可能是通过阻断ROS-p38-NF-κB通路实现的。

关键词 辛伐他汀； 高半胱氨酸,NF-κB； 内皮细胞； 活性氧

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Effects of simvastation on homocysteine-induced endothelial dysfunction and inflammatory response and its molecular mechanisms

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Abstract

<FONT face=Verdana>AIM: To investigate the effects of simvastation on homocysteine-induced endothelial dysfunction and inflammatory response and the underlying mechanisms of such effects. METHODS: MTT assay was used to detect cell viability, and DCFH-DA assay was used to examine the levels of reactive oxygen species (ROS). Furthermore, Western blotting was performed to detect protein expression and electrophoretic mobility shift assay (EMSA) was used to detect NF-κB DNA binding activity. RESULTS: Homocysteine (0.1-1 mmol/L) decreased the human umbilical vein endothelial cell (HUVEC) viability and increased the levels of ROS. Western blotting and ELISA showed that homocysteine significantly increased the expression of TNF-α, IL-6, MCP-1 and ICAM-1. However, pretreatment with simvastation (1-20 μmol/L) reversed the decreased cell viability and markedly suppressed an increase in the ROS level and the expression of TNF-α, IL-6, MCP-1 and ICAM-1 induced by homocysteine. Homocysteine induced p38 phosphorylation and such phosphorylation was also inhibited by simvastation and antioxidant NAC. EMSA and Western blotting showed that homocysteine induced NF-κB activation due to the increased phosphorylation of the inhibitory protein (IκBα) as well as the degradation of IκBα, while simvastation pretreatment almost completely blocked the NF-κB activation as well as the phosphorylation and degradation of IκBα. CONCLUSION: Simvastation inhibits homocysteine-induced endothelial dysfunction and inflammatory response through interfering with ROS-p38-NF-κB pathway.
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Key words Simvastation Homocysteine NF-kappa B； Endothelial cells Reactive oxygen species

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