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论著

舒尼替尼经线粒体内活性氧引起心肌细胞凋亡

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摘要 **目的** 探讨舒尼替尼引起心肌细胞凋亡的作用机制。**方法** H9C2细胞分别用舒尼替尼0.1, 1和10 μmol·L^{-1}处理24, 48, 72 h, MTT法测定细胞存活率; 流式细胞仪分别测定处理24 h细胞的凋亡、细胞内活性氧(ROS)、线粒体膜电位(ΔΨm)水平及胱天蛋白酶3活性。**结果** 与同一时间点正常对照组相比, 舒尼替尼1, 10 μmol·L^{-1}处理24, 48, 72 h后, 细胞存活率分别明显下降了22%和32%(24 h); 41%和68%(48 h); 62%和82%(72 h)(P<0.05)。与正常对照组相比, 舒尼替尼1, 10 μmol·L^{-1}作用24 h后, 心肌细胞内ROS水平显著升高(4.41±0.76 *vs* 8.68±0.74, 3.57±1.45)(P<0.05), 线粒体膜电位下降(309±6 *vs* 244±28, 174±2)(P<0.05), 胱天蛋白酶3活性升高(0.96±0.13 *vs* 59.40±13.17, 79.90±0.06)(P<0.05)及细胞凋亡率增加〔(6.03±0.40)% *vs* (21.05±5.55)%, (59.05±4.62)%〕(P<0.05)。**结论** 舒尼替尼可通过诱导心肌细胞内ROS的产生, 经线粒体内途径引起心肌细胞凋亡。

关键词 舒尼替尼 细胞, 培养的 心肌细胞 细胞凋亡

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Mitochondrial reactive oxygen species in sunitinib induced cardiomyocytes apoptosis

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Abstract

OBJECTIVE To investigate the cardiac toxicity of sunitinib. **METHODS** H9C2 cells were exposed to sunitinib 0.1, 1 and 10 μmol·L^{-1} for 24, 48 and 72 h. Cell viability was determined by MTT assay. Apoptosis, the level of intracellular reactive oxygen species (ROS), mitochondrial membrane potential (ΔΨm) and caspase 3 activity were detected by flow cytometry in the 24 h treatment group. **RESULTS** Compared with normal control group, sunitinib 1 and 10 μmol·L^{-1} significantly decreased cells viability by 22% and 32% for 24 h treatment group, by 48% and 68% for 48 h treatment group, and by 62% and 82% for 72 h treatment group (P<0.05). Compared with normal control group, sunitinib 1 and 10 μmol·L^{-1} significanty increased the level of intracellular ROS (4.41±0.76 *vs* 8.68±0.74, 3.57±1.45; P<0.05), significantly decreased the ΔΨm (309±6 *vs* 244±28, 174±2)(P<0.05), increased caspase 3 activity (0.96±0.13 *vs* 59.40±13.17, 79.90±0.06)(P<0.05), and decreased cell apoptosis 〔(6.03±0.40)% *vs* (21.05±5.55)%, (59.05±4.62)%〕(P<0.05). **CONCLUSION** Sunitinib could prompt the apoptosis of H9C2 cells through mitochondrial pathway by generating intracellular ROS.

Key words sunitinib cells cultured H9C2 cells apoptosis

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