药学学报 2008, 43(10) 1003-1010 DOI: ISSN: CN:

论文

SIRT1去乙酰化酶抑制剂引起人乳腺癌MCF-7耐药细胞凋亡的机制

李咏;徐榕;张秀敏;李电东;何琪杨

中国医学科学院、北京协和医学院 医药生物技术研究所， 北京 100050

摘要：

研究SIRT1去乙酰化酶抑制剂引起人乳腺癌MCF-7耐多柔比星(doxorubicin，DOX)细胞及其敏感细胞凋亡的机制。MTT法检测细胞生长抑制作用；Western blotting方法检测蛋白表达；DNA特异染料Hoechst 33342染色检测染色质凝集；Annexin V检测细胞凋亡；流式细胞仪测定细胞周期分布。结果表明，SIRT1去乙酰化酶抑制剂烟酰胺(nicotinamide，NAM)和Sirtinol对人乳腺癌细胞MCF-7敏感和耐药细胞表现出相同的生长抑制作用，但没有增强DOX活性的作用。NAM使MCF-7和MCF-7/DOX细胞阻滞在G_2/M期。50 mmol·L^{-1} NAM作用MCF-7细胞后，激活caspase凋亡通路，出现PARP、 caspase-6、 -7、 -9切割片段，并且染色质发生凝集和Annexin V阳性细胞。而在MCF-7/DOX耐药细胞中，NAM作用24 h后，才开始出现PARP、 caspase-6、 -7切割片段， 48 h后明显增加，可以检测到较多的细胞出现染色质凝集和Annexin V阳性细胞。SIRT1去乙酰化酶抑制剂对人乳腺癌MCF-7耐药细胞和敏感细胞均有相似的抑制作用，无交叉耐药性，其作用通过激活caspase凋亡通路实现。

关键词： SIRT1去乙酰化酶抑制剂 多药耐药性 细胞凋亡 人乳腺癌MCF-7细胞

Mechanism of apoptosis induced by SIRT1 deacetylase inhibitors in human breast cancer MCF-7 drug-resistant cells

LI Yong; XU Rong; ZHANG Xiu-min; LI Dian-dong; HE Qi-yang

Abstract:

The mechanism of apoptosis induced by SIRT1 deacetylase inhibitors in both human breast cancer MCF-7 and MCF-7 doxorubicin-resistant cells was studied. MTT assay was used to detect growth-inhibitory effect on the cells. Protein expression was detected by Western blotting. Chromatin condensation was detected by a fluorescent microscope after Hoechst 33342 staining. Cell cycle distribution was analyzed with flow cytometry. Apoptotic cells were detected with Annexin V staining. Nicotinamide (NAM) and Sirtinol, two SIRT1 deacetylase inhibitors, exhibited the similar growth-inhibitory effects on MCF-7/DOX cells and MCF-7 cells, but no potentiation of DOX activities. The arrest at G_2/M phase was detected by flow cytometry in both MCF-7 and MCF-7/DOX cells after NAM treatment. Activation of caspase pathway in MCF-7 cells, such as the cleavages of PARP, caspase-6, -7, -9, were observed after exposure to NAM 50 mmol·L^{-1}, accompanied by the occurrence of chromatin condensation and Annexin V positive cells. However, the cleavages of PARP, caspase-6 and -7 in MCF-7/DOX cells delayed after exposure to NAM for 24 h and obviously increased at 48 h with appearance of chromatin condensation and Annexin V positive cells. SIRT1 deacetylase inhibitors show no cross resistance to MCF-7 drug-resistant cells, and the similar growth-inhibitory actions of them to MCF-7 sensitive and drug-resistant cells by which it is mediated by activation of apoptotic caspase pathway.

Keywords: multidrug resistance apoptosis human breast MCF-7 cancer cell SIRT1 deacetylase inhibitor

收稿日期 2008-04-22 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 何琪杨

作者简介:

参考文献：

本刊中的类似文章

文章评论 (请注意:本站实行文责自负, 请不要发表与学术无关的内容!评论内容不代表本站观点.)

反馈人		邮箱地址	
反馈标题		验证码	7273