140~144.蛋白酶体抑制剂MG-132逆转人结肠癌细胞获得性TRAIL耐药[J].胡静姿,朱洪波,何 超,劳伟峰,黄学锋.中国肿瘤生

蛋白酶体抑制剂MG-132逆转人结肠癌细胞获得性TRAIL耐药

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基金项目：国家自然科学基金资助项目（No.30700970）；浙江省自然科学基金资助项目（No.Y205093）

DOI：10.3872/j.issn.1007-385X.2009.2.008

摘要：

目的: 探讨蛋白酶体抑制剂MG 132逆转人结肠癌细胞获得性TRAIL耐药的作用及其可能的机制。方法：在MG 132和TR
肠癌细胞DLD1 TRAIL/R后，MTT法检测细胞的存活率，流式细胞术检测细胞凋亡率，Western blotting检测细胞中各种凋
平。结果：MG 132联合TRAIL蛋白处理DLD1 TRAIL/R细胞后，其细胞存活率明显下降（ P <0.01），而细胞凋亡率则
otting检测显示，联合处理后DLD1 TRAIL/R细胞中各种凋亡信号分子包括caspase 8、caspase 9、caspase 3、Bid和
C和Smac蛋白大量释放；进一步的Western blotting检测显示，死亡受体DR5和凋亡诱导蛋白Bik的表达水平明显增高，而
k、Bcl XL、XIAP和Survivin等则无明显改变；检测结果还显示，MG 132能诱导JNK激酶发生磷酸化，使用JNK激酶抑制剂
表达，但不影响Bik的表达，并且不能减弱MG 132和TRAIL蛋白联合处理对DLD1 TRAIL/R细胞的致凋亡效应（ P <0.0
转人结肠癌细胞DLD1 TRAIL/R的获得性TRAIL耐药，其机制可能与Bik蛋白上调后启动线粒体凋亡途径有关，与JNK通路激

关键词：蛋白酶体抑制剂 MG-132 结肠肿瘤细胞 TRAIL 耐药 Bik

Proteasome inhibitor MG-132 reverses acquired resistance to TRAIL in human colon cancer cells

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Fund Project:Supported by the National Natural Science Foundation of China(No. 30700970); the Natu
Province(No. Y205093)

Abstract:

Objective: To evaluate the role of proteasome inhibitor MG 132 in reversing the acquired TRAIL resist
line DLD1 TRAIL/R and the related mechanisms. Methods:Colon cancer cell line DLD1 TRAIL/R was tr
TRAIL protein. The viability of DLD1 TRAIL/R cells was determined by MTT assay; the apoptotic rate w
the expression of apoptosis related proteins was examined by Western blotting analysis. Results: The via
dramatically decreased after combined treatment with MG 132 and TRAIL protein(P <0.01) and the ap
increased (P <0.01). Western blotting analysis showed that MG 132 dramatically enhanced the cleava
including caspases 8, 9, 3, Bid, and PARP in DLD1 TRAIL/R cells after combined treatment and increased
Smac from mitochondria. Further study demonstrated that MG 132 up regulated DR5 and Bik proteins, b
Bax, Bak, Bcl XL, XIAP or survivin. Moreover, we found MG 132 induced phosphorylation of kinase JNK, an
blocked MG 132 induced expression of DR5, but not the expression of Bik. Furthermore, SP600125 did n
TRAIL/R cells induced by MG132 in the presence of TRAIL protein (P <0.05). Conclusion: Proteasome i
acquired drug resistance to TRAIL and induce up regulation of DR5 and Bik protein in DLD1 TRAIL/R cells.
involve the initiation of mitochondrion related apoptosis caused by Bik protein expression, not by activat

Keywords:proteasome inhibitor MG 132 colonic neoplasms cell TRAIL resistance Bik

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