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论文

抗癌抗生素力达霉素诱导人肝癌BEL-7402细胞死亡的特征

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摘要：

目的 研究抗癌抗生素力达霉素(LDM)诱导人肝癌BEL-7402细胞死亡的特征。方法用荧光染料Hoechst 33342和PI联染；琼脂糖凝胶电泳检测；流式细胞术检测等。结果 LDM1μmol.L^{-1}处理该细胞后6h，可观察到一种有别于典型凋亡的染色质凝集方式：核膜一直保持完整，细胞仍贴壁，无凋亡小体形成；琼脂糖凝胶电泳检测到DNA梯带。流式细胞术检测到的G1亚峰，仅在LDM处理BEL-7402细胞后24h出现。LDM处理BEL-7402细胞后6h，caspase-3，6的活性分别增高5，4倍。染色质开始凝集的时间比caspase-6活性达到高峰的时间早。结论 力达霉素诱导人肝癌BEL-7402细胞死亡的特征有别于典型的凋亡，此结果可能有助于解释其极高活性地杀死肿瘤细胞的分子机制。

关键词： 抗癌抗生素；力达霉素；人肝癌细胞；细胞死亡

CHARACTERIZATION OF CELL DEATH INDUCED BY ANTICANCER ANTIBIOTIC LIDAMYCIN IN HUMAN HEPATOMA BEL-7402 CELLS

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Abstract:

AIM To study the features of cell death induced by the anticancer antibiotic lidamycin (LDM) in human hepatoma BEL-7402 cells. METHODS Chromatin condensation was observed by co-staining with fluorescent dyes, hoechst 33342 and propidium iodide. “G1 sub-peak” was detected by flow cytometry and DNA ladder was observed using agarose gel electrophoresis. The caspase-3, 6 activities were measured with kits specific for them. RESULTS Typical apoptotic chromatin condensations appeared when the BEL-7402 cells were treated with the conventional antitumor agent mitomycin C 30 μmol.L^{-1} for 12 h. However, an abnormal type of chromatin condensation occurred when the cells were treated with LDM 1 μmol.L^{-1} for 6 h, which was characterized with keeping the completeness of nuclear membrane and not forming apoptotic bodies. The DNA ladder patterns were observed using agarose gel electrophoresis. The “G1 sub-peak” occurred only in the cells treated with LDM for 24 h, though chromatin condensation was earlier detected in treatment with LDM for 6 h. The caspase-3, 6 activities were increased about 5 and 4 folds, after the cells were treated with LDM 1 μmol.L^{-1} for 6 h, as did mitomycin C. The time of initiating chromatin condensation was earlier than that of the high peak activities of caspase-6. CONCLUSION The characterization of cell death induced by lidamycin in the human hepatoma BEL-7402 cells differs from typical apoptosis. The results make it helpful to explain the molecular mechanism of the highly potent cytotoxicities of lidamycin toward tumor cells.

Keywords: lidamycin human hepatoma BEL-7402 cells cell death anticancer antibiotic

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