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基础研究

分割剂量电离辐射对卵巢癌耐药细胞自噬性死亡的影响

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摘要：

目的：研究不同电离辐射方式对卵巢癌耐药细胞株SKVCR自噬性细胞死亡的影响，并探讨其相关机制。方法：实验分为假照组、分割照射组(2 Gy•d^{-1}×5)及单次照射组(10 Gy•d-1×1)。采用MTT法检测各组细胞对长春新碱（VCR）、依托泊苷（VP-16）及顺铂（DDP）的药物敏感性，MDC染色及流式细胞术检测自噬发生率的变化，实时荧光定量PCR方法检测自噬特异基因MAPLC3B和Akt1 mRNA水平，Western blotting法检测自噬相关蛋白MAPLC3B表达和蛋白激酶B(PKB，Akt1)/哺乳动物雷帕霉素靶蛋白(mTOR)及其下游基因P70 S6K、磷酸化AKT1/mTOR/P70 S6K表达的变化。结果：与假照组比较,电离辐射使SKVCR细胞对VCR、VP-16的药物敏感性提高，分割照射组更明显(P<0.05)。与假照组比较，电离辐射使细胞自噬发生率升高，尤其以分割照射组升高更明显(P<0.05)；与假照组比较，照射后MAPLC3B mRNA升高、Akt1 mRNA下降(P<0.05)； 照射后MAPLC3B蛋白表达升高，Akt1、mTOR、p-mTOR、P70 S6K、p-P70 S6K蛋白表达均不同程度下降，分割照射组较单次照射组下降更明显(P<0.05)。结论：不同的电离辐射作用方式可以引起卵巢癌细胞发生自噬性死亡，其机制主要涉及Akt1/mTOR/S6K通路。

关键词： 原代海马神经元；视黄酸；视黄酸核受体α；钙兴奋性；基因沉默

Calcium excitability of rat primary hippocampal neuron damaged by silenced retinoic acid receptor α

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Abstract:

To study the necessary of retinoic acid receptor α (RARα) for rat neuron function.
Methods Tissue digestion was used to isolate and cultivate the rat primary hippocampal neurons,and the adenovirus vector was used to specifically silence the RARα;Real-Time PCR was used to analyze the influence of silenced RARα in retinoic acid(RA) receptors and the markers of nerve cells;live cell imaging analysis was performed to analyze the influence of the calcium excitability of neurons silenced RARα.Results The immunofluorescence results showed that 90% of the isolated cells expressed the neuron marker neuron-specific enolase (NSE),the adenoviral transfection efficiency was up to 80%.The PCR results showed the expression of RARα in silenced RARα neuron was decreased by 75% (P<0.01),the other receptors were significantly decreased (P<0.01),but RARβ was significantly increased (P<0.05).The live cell calcium imaging results showed the calcium excitability in silent group was significantly reduced (P<0.05),however all-trans retinoic acid (ATRA) pretreatment for 24 h could significantly enhance the calcium excitability (P<0.01).Conclusion The absence of RARα can significantly reduce the neuron marker NSE expression of the primary hippocampal neurons,and significantly damage the neuronal calcium excitability.

Keywords: primary hippocampal neurons；retinoic acid；retinoic acid receptor α；calcium excitability；gene silence

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