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基础研究

碘-125对胶质瘤SHG-44细胞的细胞程序性死亡作用及相关基因表达的影响

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摘要：

目的：观察碘-125（125I）粒子对体外培养的人脑恶性胶质瘤细胞系SHG-44的生长抑制及诱导细胞程序性死亡作用，阐明此过程中相关基因的作用机制。方法：人脑恶性胶质瘤细胞株SHG-44，根据应用125I粒子剂量不同分为对照组与处理组，采用四甲基偶氮唑蓝(MTT)法检测125I粒子对SHG-44细胞增殖率的影响；用电镜和原位凋亡检测法(TUNEL)及流式细胞仪、吖啶噔／溴乙啶双荧光染色检测细胞程序性死亡改变，应用基因芯片技术筛选出处理前后与细胞程序性死亡有关的表达差异有统计学意义的基因。结果：125I粒子作用于体外培养的SHG-44胶质瘤细胞，产生了剂量、时间依赖性的增殖抑制作用。MTT比色法检测，经125I粒子处理的SHG-44人胶质瘤细胞，随放射剂量的增加和作用时间的延长，A值明显降低。经2粒125I粒子作用3 d（累积剂量86.8 MBq）抑制率约为50%，与对照组比较差异有显著性（P<0.05）。透射电镜下观察到处理后SHG44胶质瘤细胞中频繁细胞自噬现象。流式细胞仪检测，S期细胞数在作用后逐渐减少，而G1期和 G2/M期细胞比例显著增加。虽然细胞中凋亡细胞的比例随时间的延长有所增加，但比例未超过2%。筛选出SHG-44胶质瘤细胞在125I粒子作用前后差异表达且与程序性死亡相关的基因共56条(上调 36条，下调20条)。结论：125I粒子以剂量、时间依赖性方式通过细胞程序性死亡来抑制胶质瘤细胞的增殖，促进细胞向凋亡方向转化；125I粒子诱导下的细胞系中还存在非凋亡调控的细胞程序性死亡(自噬)；胶质瘤细胞凋亡过程中相关基因p53/ATM通路的基因、c-myc家族、p16、Bcl-2家族等参与诱导胶质瘤细胞程序性死亡的发生机制。

关键词： 星形细胞瘤； 碘-125;基因芯片

Effects of 125I on programmed cell death and expressions of genes related to programmed cell death in glioma cell line SHG-44

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Abstract:

Abstract:Objective To investigate the effects of 125I seed on the growth and programmed cell death of human glioma cell line SHG-44,and clarify the action mechanism of the related genes in this process. Methods SHG-44 glioma cells were cultivated in vitro, and divided into control group and treatment group.The inhibitory effect of 125I on SHG-44 cell proliferation was determined by MTT method. The morphological changes of SHG-44 cells were examined by electron microscopy, TUNEL method and Acridine Orange/Ethidium bromide double fluorescent staining. The gene expresion profile was established by using gene chip technique. Results 125I seed had inhibitory effect on the proliferation of SHG-44 cells cultivated in vitro in a dose and time-dependent manner.The result of MTT showed that the A value of SHG-44 cells treated with 125I seed was significantly decreased with the increasing of radiation dose and prolongation of time.The inhibitory rate of SHG-44 cells after treated with 125I seed for 3 d was 50%,there was significant difference compared with control group(P<0.05). Autophagy was frequently observed under transmission electron microscope in SHG-44 cells.The number of cells at S phase was reduced while the number of cells at G1 and G2/M phase was increased.Although the apoptosis in SHG-44 cells was increased,but not more than 2%. There were 56 differential expression genes of SHG-44 cells after exposure to 125I including 36 up-regulation genes and 20 down-regulation genes. Conclusion 125I seed can inhibit the proliferation of SHG-44 glioma cells in a dose-dependent manner by inducing the programmed cell death. There may be non-apoptotic programmed cell death (autophagy) in SHG-44 glioma cell line after induction by 125I at relatively low concentration. These results suggest that the mechanism of 125I-induced proliferation inhibitory effect and apoptosis in SHG-44 cells may be related to the genes of p53 and ATM pathway，C-myc family ,p16 family ,Bcl-2 family，TNF ligand family and TNF receptor family genes.

Keywords: astrocytoma iodine-125;gene chip

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