替莫唑胺通过调控miR-216a/PRKCA抑制胶质瘤细胞U251增殖和侵袭作用的研究

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Title: **Inhibitory effect of temozolomide on proliferation and invasion of glioma cell line U251 by regulating miR-216a/PRKCA**

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关键词: 替莫唑胺; miR-216a; PRKCA; 胶质瘤细胞U251; 增殖; 侵袭

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摘要: 目的：探讨替莫唑胺抑制胶质瘤细胞U251增殖和侵袭的作用，推测其作用机制是通过微小RNA-216a（microRNA-216a，miR-216a）/蛋白激酶Cα(protein kinase C-alpha，PRKCA)进行调控。方法：体外培养胶质瘤细胞U251，用不同剂量替莫唑胺染毒48 h后，构建野生型PRKCA 3' UTR-荧光素酶报告载体及检测荧光素酶活性，检测替莫唑胺对胶质瘤细胞U251增殖和侵袭的影响及miR-216a和PRKCA表达的影响。结果:miR-216a mimics使野生型PRKCA 3' UTR-荧光素酶报告载体的活性下降了47.52%，差异具有统计学意义（P < 0.05）；miR-216a mimics使突变型PRKCA 3' UTR-荧光素酶报告载体的活性下降不显著，差异无统计学意义（P > 0.05）。与空白对照组比较，低、中、高剂量组胶质瘤细胞U251增殖率、侵袭细胞数、PRKCA mRNA相对表达量和PRKCA蛋白表达量均降低，miR-216a mRNA相对表达量均增高，差异具有统计学意义（P < 0.05）；随着替莫唑胺剂量的增加，胶质瘤细胞U251增殖率、侵袭细胞数、PRKCA mRNA相对表达量和PRKCA蛋白表达量随之降低，miR-216a mRNA相对表达量随之增高，差异具有统计学意义（P < 0.05）。结论：替莫唑胺可以通过促进miR-216a的表达而抑制PRKCA的表达，降低胶质瘤细胞U251增殖和侵袭。

Abstract: Objective:To investigate the inhibitory effect of temozolomide on proliferation and invasion of glioma cell line U251 by regulating microRNA-216a/protein kinase C-α (miR-216a/PRKCA).Methods:In this study,the glioma cell line U251 cultured in vitro exposed to different doses of temozolomide for 48 h were used to construct the wild type PRKCA 3' untranslated region (UTR)-luciferase vector,which could be used for the luciferase activity detection,then the effect of temozolomide on proliferation and invasion of glioma cell U251 and the expression of miR-216a and PRKCA were analyzed.Results:MiR-216a mimics could bind to the wild type PRKCA 3' UTR and inhibited the luciferase activity by 47.52%(P < 0.05).The decrease in the luciferase activity of mutant type PRKCA 3' UTR caused by miR-216a mimics was not obvious (P > 0.05).The proliferation rate of U251,number of invasive cells,relative expression of PRKCA mRNA and PRKCA protein in the glioma cells cultured in the low,middle and high dose groups were lower than those of the blank control group (P < 0.05).The relative expression level of miR-216a mRNA was higher in the three different dose groups than in the blank control group (P < 0.05).With the increase of the temozolomide dosage,the proliferation rate of U251,number of invasive cells,relative expression of PRKCA mRNA and PRKCA protein in the glioma cells showed a decrease trend,while the relative expression level of miR-216a mRNA showed an increase trend (P < 0.05).Conclusion:Temozolomide can inhibit the expression of PRKCA and reduce the proliferation and invasion of glioma cell U251 by promoting the expression of miR-216a.

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