扁塑藤素抑制人胶质母细胞瘤U251细胞增殖的机制探讨

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Title: The mechanism of pristimerin inhibits proliferation of human glioblastoma U251 cells

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关键词: 扁塑藤素; 胶质母细胞瘤; 细胞增殖; PI3K/AKT信号通路

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摘要: 目的：探讨扁塑藤素对人胶质母细胞瘤U251细胞增殖的影响及其机制。方法：2、4和8 μmol/L的扁塑藤素作用U251细胞24 h后，使用四甲基偶氮唑蓝（MTT）法检测U251细胞活力；Cell cycle staining Kit检测U251细胞周期；免疫印迹法检测增殖细胞核抗原（PCNA）蛋白和p-PI3K、PI3K、p-AKT以及AKT蛋白表达。结果：2、4和8 μmol/L的扁塑藤素显著降低U251细胞的活力，且具有浓度依赖性。扁塑藤素可下调U251细胞PCNA蛋白的表达。扁塑藤素处理U251细胞后，G1期细胞数明显增加，S期细胞数明显减少。扁塑藤素处理可明显降低U251细胞p-PI3K/PI3K、p-AKT/AKT的比值。结论：扁塑藤素可能通过抑制PI3K/AKT信号通路的活化抑制人胶质母细胞瘤的细胞增殖。

Abstract: Objective：To explore the impact of pristimerin on cell proliferation of U251 cells.Methods：After treating with different concentrations of pristimerin（2，4，8 μmol/L) for 24 h，the viability of U251 cells was measured using MTT assay.Cell cycle was detected by cell cycle staining Kit.The expression levels of PCNA（proliferating cell nuclear antigen)，p-PI3K，PI3K，p-AKT and AKT were determined by Western blot.Results：Compared with the control group，pristimerin markedly reduced the cell viability of U251 in a dose dependent way.Additionally，the expression levels of PCNA protein were obviously downregulated in pristimerin-treated U251 cells.We also found that the cell numbers in G1 period were obviously increased while the cell numbers in S period were markedly decreased in U251 cells treated by pristimerin.Eventually，the ratios of p-PI3K/PI3K and p-AKT/AKT were markedly reduced in pristimerin-treated U251 cells.Conclusion：Pristimerin can inhibit cell proliferation of human glioblastoma by inhibiting the activation of PI3K/AKT signalling.

参考文献/REFERENCES

[1]Ostrom QT，Gittleman H，de Blank PM，et al.American brain tumor association adolescent and young adult primary brain and central nervous system tumors diagnosed in the united states in 2008-2012［J］.Neuro Oncol，2016，18（Suppl 1）：i1-i50.
[2]Mcneill KA.Epidemiology of brain tumors［J］.Neurologic Clinics，2016，34(4)：981.
[3]Wen PY，Kesari S.Malignant gliomas in adults［J］.N Engl J Med，2008，359(5)：492-507.
[4]Filho WB，Corsino J，Bolzani VDS，et al.Quantitative determination of cytotoxic?Friedo-nor-oleanane derivatives from five morphological types of Maytenus ilicifolia（celastraceae)by reverse-phase high-performance liquid chromatography［J］.Phytochem Anal，2002，13(2)：75-78.
[5]Liu Y，Gao X，Deeb D，et al.Anticancer agent pristimerin inhibits IL-2 induced activation of T lymphocytes［J］.J Exp Ther Oncol，2016，11(3)：181-188.
[6]Cevatemre B，Erkisa M，Aztopal N，et al.A promising natural product，pristimerin，results in cytotoxicity against breast cancer stem cells in vitro and xenografts in vivo through apoptosis and an incomplete autopaghy in breast cancer［J］.Pharmacol Res，2018，129：500-514.
[7]Zhang B，Zhang J，Pan J.Pristimerin effectively inhibits the malignant phenotypes of uveal melanoma cells by targeting NFkappaB pathway［J］.Int J Oncol，2017，51(3)：887-898.

[8]Guo Y，Zhang W，Yan YY，et al.Triterpenoid pristimerin induced HepG2 cells apoptosis through ROS-mediated mitochondrial dysfunction［J］.J BUON，2013，18(2)：477-485.
[9]Zhao H，Wang C，Lu B，et al.Pristimerin triggers AIF-dependent programmed necrosis in glioma cells via activation of JNK［J］.Cancer Lett，2016，374(1)：136-148.
[10]Yousef BA，Hassan HM，Zhang LY，et al.Pristimerin exhibits in vitro and in vivo anticancer activities through inhibition of nuclear factor-small ka，CyrillicB signaling pathway in colorectal cancer cells［J］.Phytomedicine，2018，40：140-147.
[11]Chan KKL，Siu MKY，Jiang YX，et al.Estrogen receptor modulators genistein，daidzein and ERB-041 inhibit cell migration，invasion，proliferation and sphere formation via modulation of FAK and PI3K/AKT signaling in ovarian cancer［J］.Cancer Cell Int，2018，18(1)：65.
[12]Zheng J，Zhang M，Zhang L，et al.HSPC159 promotes proliferation and metastasis via inducing EMT and activating PI3K/Akt pathway in breast cancer［J］.Cancer Sci，2018，3：1-11.
[13]Cheng F，Yang Z，Huang F，et al.MicroRNA-107 inhibits gastric cancer cell proliferation and metastasis by targeting PI3K/AKT pathway［J］.Microb Pathog，2018，121：110-114.
[14]Li R，Chen X，You Y，et al.Comprehensive portrait of recurrent glioblastoma multiforme in molecular and clinical characteristics［J］.Oncotarget，2015，6(31)：30968-30974.
[15]Cuddapah VA，Robel S，Watkins S，et al.A neurocentric perspective on glioma invasion［J］.Nat Rev Neurosci，2014，15(7)：455-465.
[16]Liu YB，Gao X，Deeb D，et al.Role of telomerase in anticancer activity of pristimerin in prostate cancer cells［J］.J Exp Ther Oncol，2017，11(1)：41-49.
[17]Yousef BA，Guerram M，Hassan HM，et al.Pristimerin demonstrates anticancer potential in colorectal cancer cells by inducing G1 phase arrest and apoptosis and suppressing various pro-survival signaling proteins［J］.Oncol Rep，2016，35(2)：1091-1100.
[18]Zuo J，Guo Y，Peng X，et al.Inhibitory action of pristimerin on hypoxiamediated metastasis involves stem cell characteristics and EMT in PC-3 prostate cancer cells［J］.Oncol Rep，2015，33(3)：1388-1394.
[19]Jur□-Kov□ M，Danihel □，Pol□ k□，et al.Ki67，PCNA，and MCM proteins：Markers of proliferation in the diagnosis of breast cancer［J］.Acta Histochemica，2016，118(5)：544-552.
[20]Yang M，Zhai X，Xia B，et al.Long noncoding RNA CCHE1 promotes cervical cancer cell proliferation via upregulating PCNA［J］.Tumor Biology，2015，36(10)：7615-7622.
[21]Hengstschl□ger M，Braun K，Soucek T，et al.Cyclin-dependent kinases at the G1-S transition of the mammalian cell cycle［J］.Mutation Research，1999，436(1)：1-9.
[22]Yan YY，Bai JP，Xie Y，et al.The triterpenoid pristimerin induces U87 glioma cell apoptosis through reactive oxygen species-mediated mitochondrial dysfunction［J］.Oncology Letters，2013，5(1)：242-248.
[23]Carnero A，Paramio JM.The PTEN/PI3K/AKT pathway in vivo，cancer mouse models［J］.Front Oncol，2014，4：252.
[24]Geng Junhui，Zhang Lijun，Wang Yali，et al.The progress of PI3K/Akt signaling pathway and tumor angiogenesis［J］.Modern Oncology，2018，26（09）：1462-1466.［耿军辉，张丽军，王亚丽，等.PI3K/Akt信号通路与肿瘤血管新生的研究进展［J］.现代肿瘤医学，2018，26（09）：1462-1466.］
[25]Xu C，Sun G，Yuan G，et al.Effects of platycodin D on proliferation，apoptosis and PI3K/Akt signal pathway of human glioma U251 cells［J］.Molecules，2014，19(12)：21411-21423.
[26]Chang Y，Wu Q，Tian T，et al.The influence of SRPK1 on glioma apoptosis，metastasis，and angiogenesis through the PI3K/Akt signaling pathway under normoxia［J］.Tumour Biol，2015，36(8)：6083-6093.

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