冬凌草甲素上调p53转录活性促进胶质瘤细胞凋亡的作用与分子机制探讨

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Title: **Oridonin up-regulated p53 transcriptional activity promoted apoptosis of glioma cells and its molecular mechanism**

作者: 朱晗清; 高丰厚
上海交通大学医学院附属第九人民医院肿瘤科，上海 200011

Author(s): Zhu Hanqing; Gao Fenghou
Department of Oncology，Shanghai 9th People's Hospital，Shanghai Jiaotong University School of Medicine，Shanghai 200011，China.

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摘要: 目的：探讨冬凌草甲素抑制胶质瘤细胞U-87 MG、A-172活性的分子机制。方法：CCK8法检测不同浓度的冬凌草甲素对胶质瘤细胞U-87 MG、A-172活力的影响。选择20 μmol/L的冬凌草甲素分别处理胶质瘤细胞U-87 MG、A-172 0、6、12 h后，Western blotting法检测p53及其下游p21、Bax蛋白的表达情况，同时检测Cleaved PARP、Cleaved Caspase3的表达情况，实时荧光定量PCR法检测p53 mRNA水平的改变。应用p53转录活性抑制剂Pifithrin-α（PFT-α)预处理胶质瘤细胞U-87 MG 24 h后，Western blotting法检测冬凌草甲素对p53及其下游蛋白、Cleaved PARP、Cleaved Caspase3表达情况的影响。结果：冬凌草甲素对U-87 MG、A-172细胞的活性具有明显的抑制作用，冬凌草甲素作用24 h对胶质瘤细胞U-87 MG、A-172的IC50均介于20~30 μmol/L。冬凌草甲素可以上调p53及其下游p21、Bax蛋白并具有时间依赖性，而不改变p53的mRNA水平。此外，冬凌草甲素可以诱导胶质瘤细胞U-87 MG、A-172凋亡。p53转录活性抑制剂可以废除冬凌草甲素对p53及其下游p21、Bax蛋白的上调作用，同时也减弱了冬凌草甲素对胶质瘤细胞U-87 MG的促凋亡作用。结论：冬凌草甲素可能通过上调p53蛋白表达、增强其转录活性，促进胶质瘤细胞凋亡，而对胶质瘤细胞活性产生抑制效应。

Abstract: Objective：To explore the molecular mechanism of oridonin inhibiting the activity of glioma U-87 MG and A-172 cells.Methods：CCK8 method was used to detect the effects of different concentration of oridonin on the activity of U-87 MG and A-172 cells.After U-87 MG and A-172 cells treated with 20 μmol/L oridonin for 0，6，12 h，Western blotting method was used to detect the expression of p53 and its downstream p21 and Bax protein，at the same time，the expression of Cleaved PARP and Cleaved Caspase3 was detected.After the pre-treatment of p53 transcriptional inhibitor Pifithrin-α（PFT-α) on U-87 MG，the effect of oridonin on the expression of p53 and its downstream protein，Cleaved PARP and Cleaved Caspase3 was detected by Western blotting method.Results：Oridonin had an obvious inhibitory effect on the activity of U-87 MG and A-172.IC50 of oridonin treatment for 24 h on U-87 MG and A-172 cells were between 20 and 30 μmol/L.Oridonin can up regulate p53 and its downstream p21 and Bax proteins in a time-dependent，without changing the mRNA level of p53.In addition，oridonin can induce apoptosis of U-87 MG and A-172 cells.p53 transcriptional activity inhibitor can abolish the up-regulated effect of oridonin on the p53 and its downstream p21 and Bax proteins，and also weaken the apoptosis effect of oridonin on the U-87 MG cells.Conclusion：Oridonin may promote the apoptosis of glioma cells by up-regulating the expression of p53 protein and enhancing its transcriptional activity to inhibit the activity of glioma cells.

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