葛根素通过TGF-β/Smads信号通路促进前列腺癌细胞凋亡的机制

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2020年01期 **页码:** 17-22 **栏目:** 论著（基础研究） **出版日期:** 2019-11-30

Title: **Effects of puerarin on apoptosis of prostate cancer cells through TGF-β/Smads signaling pathway**

作者: 金 蓓[1]; 黄蓉飞[2]; 刘清松[3]

1.雅安市雨城区人民医院病理科，四川 雅安 625000;2.成都医学院第一附属医院病理科，四川 成都 610500;3.内江市第一人民医院病理科，四川 内江 641000

Author(s): Jin Bei[1]; Huang Rongfei[2]; Liu Qingsong[3]

1.Department of Pathology，Ya'an Yucheng District People's Hospital，Sichuan Ya'an 625000，China；2.Department of Pathology，the First Affiliated Hospital of Chengdu Medical College，Sichuan Chengdu 610500，China；3.Department of Pathology，Neijiang First People's Hospital，Sichuan Neijiang 641000，China.

关键词: 葛根素; TGF-β/Smads; 前列腺癌; 凋亡

Keywords: puerarin; TGF-β/Smads; prostate cancer; apoptosis

分类号: R737.25

DOI: 10.3969/j.issn.1672-4992.2020.01.005

文献标识码: A

摘要: 目的：探讨葛根素（puerarin）通过TGF-β/Smads信号通路促进前列腺癌细胞凋亡的机制。方法：将不同浓度葛根素（0、25、50、75和100 μmol/L）分别孵育前列腺癌PC3细胞，并采用台盼蓝染色(trypan blue）检测细胞增殖情况；流式细胞术方法检测不同剂量葛根素对细胞凋亡率的影响；使用RT-PCR和Western blot检测葛根素对TGF-β1和Smad3的影响；采用TGF-β1抑制剂P144抑制TGF-β1活性，使用Western blot验证P144对TGF-β1表达含量的影响并检测其对细胞凋亡蛋白Casepase3、Bcl-2表达水平的影响。结果：葛根素以时间和剂量依赖的方式抑制PC3细胞的生长（P<0.05）；25、50、75和100 μmol/L葛根素对细胞存活的抑制率分别为25.7%、28.9%、32.5%和56.3%；流式细胞术检测结果指出25、50、75和100 μmol/L葛根素对PC3细胞的凋亡率分别为(4.36±2.62)%、(9.86±3.64)%、(15.95±5.22)%、(19.65±7.34)%，随着剂量的增长，PC3细胞凋亡率逐渐上升（P<0.05）；RT-PCR和Western blot检测提示随着葛根素浓度的升高，TGF-β1、Smad3和Caspase3在mRNA和蛋白水平表达含量显著升高，而Bcl-2则显著降低（P<0.05）；与葛根素单独处理组相比，葛根素+P144共处理组细胞，TGF-β1、Smad3和Caspase3蛋白表达水平显著下降，Bcl-2蛋白表达水平显著升高（P<0.05）。随后的流式细胞术检测结果指出，与葛根素单独处理组比，使用葛根素+P144共处理组细胞凋亡水平显著下降（P<0.05）。结论：葛根素可能通过激活TGF-β/Smad受体信号通路诱导Bcl-2下调和促进Caspase3的上调，从而诱导前列腺癌PC3细胞凋亡。

Abstract: Objective：To investigate the mechanism of puerarin promoting apoptosis of prostate cancer cells through TGF-β/Smads signaling pathway.Methods：Different concentrations of puerarin(0，25，50,75 and 100 μmol/L) were incubated with prostate cancer PC3 cells，respectively，and trypan blue staining was used to detect cell proliferation.Flow cytometry was used to detect different doses of puerarin.The effect of puerarin on TGF-β1 and Smad3 was detected by RT-PCR and Western blot.The expression of TGF-β1 was inhibited by TGF-β1 inhibitor P144，and the expression of TGF-β1 by P144 was confirmed by Western blot.The effect of the content and its effect on the expression levels of the apoptotic proteins Casepase3 and Bcl-2 were detected.Results：Puerarin inhibited the growth of PC3 cells in a time- and dose-dependent manner(P<0.05).The inhibition rates of 25，50，75 and 100 μmol/L puerarin were 25.7%，28.9%，32.5% and 56.3%，respectively.The results of flow cytometry indicated that the apoptosis rates of puerarin on PC3 cells were (4.36±2.62)%，(9.86±3.64)%，(15.95±5.22)%，(19.65±7.34)%.With the increase of dose，the apoptosis rate of PC3 cells increased gradually(P<0.05).RT-PCR and Western blot showed that with the concentration of puerarin elevated，TGF-β1，Smad3 and Caspase3 were highly expressed at mRNA and protein levels significantly，while Bcl-2 was

significantly decreased(P<0.05).Compared with puerarin alone，the expression of TGF-β1，Smad3 and Caspase3 protein was significantly decreased in puerarin+P144 co-treatment group，Bcl-2 protein expression level was significantly increased(P<0.05).The results of subsequent flow cytometry showed that the apoptosis level of cells treated with puerarin+P144 was significantly lower than that of puerarin alone(P<0.05).Conclusion：Puerarin can induce apoptosis of PC3 cells by inducing down-regulation of anti-apoptotic protein and activation of Caspase3 by activating TGF-β/Smad receptor signaling pathway.

参考文献/REFERENCES

[1] Zhang Q，Hong B，Wu S，et al.Inhibition of prostatic cancer growth by ginsenoside Rh2 [J] .Tumor Biology，2015，36(4)：2377-2381.
[2] Gundem G，Van Loo P，Kremeyer B，et al.The evolutionary history of lethal metastatic prostate cancer [J] .Nature，2015，520(7547)：353.
[3] Chen W，Zheng R，Baade PD，et al.Cancer statistics in China，2015 [J] .CA：A Cancer Journal for Clinicians，2016，66(2)：115-132.
[4] Fournier PGJ，Juárez P，Jiang G，et al.The TGF-β signaling regulator PMEPA1 suppresses prostate cancer metastases to bone [J] .Cancer Cell，2015，27(6)：809-821.
[5] Hu Q，Tong S，Zhao X，et al.Periostin mediates TGF-β-induced epithelial mesenchymal transition in prostate cancer cells [J] .Cellular Physiology and Biochemistry，2015，36(2)：799-809.
[6] Seoane J，Gomis RR.TGF-β family signaling in tumor suppression and cancer progression [J] .Cold Spring Harbor Perspectives in Biology，2017，2(02)：277.
[7] Yang F，Chen Y，Shen T，et al.Stromal TGF-β signaling induces AR activation in prostate cancer [J] .Oncotarget，2014，5(21)：10854.
[8] Yuan J，Yang F，Wang F，et al.A long noncoding RNA activated by TGF-β promotes the invasion-metastasis cascade in hepatocellular carcinoma [J] .Cancer cell，2014，25(5)：666-681.
[9] Li C，Wang Z，Wang Q，et al.Enhanced anti-tumor efficacy and mechanisms associated with docetaxel-piperine combination-in vitro and in vivo investigation using a taxane-resistant prostate cancer model [J] .Oncotarget，2018，9(3)：3338.
[10] Liu X，Zhao W，Wang W，et al.Puerarin suppresses LPS-induced breast cancer cell migration，invasion and adhesion by blockage NF-κB and Erk pathway [J] .Biomedicine & Pharmacotherapy，2017，92(05)：429-436.
[11] Meng XP，Zhang Z，Wang YF，et al.Evaluation of anti-hepatocarcinoma capacity of puerarin nanosuspensions against human HepG2 cells [C] //Biophotonics and Immune Responses XII.International Society for Optics and Photonics，2017 (10065) ：100650U.
[12] Tamaki H，Harashima N，Hiraki M，et al.Bcl-2 family inhibition sensitizes human prostate cancer cells to docetaxel and promotes unexpected apoptosis under caspase-9 inhibition [J] .Oncotarget，2014，5(22)：11399.
[13] Li Y，Luo W，Li G，et al.Genistein induced apoptosis of gastric cancer cell through Bcl-2 and Caspase-3 regulation [J] .Clin Oncology，2016，51(1)：1150-1156.
[14] K Kontos C，Christodoulou MI，Scorilas A.Apoptosis-related BCL2-family members：Key players in chemotherapy [J] .Anti-Cancer Agents in Medicinal Chemistry(Formerly Current Medicinal Chemistry-Anti-Cancer Agents)，2014，14(3)：353-374.
[15] David CJ，Huang YH，Chen M，et al.TGF-β tumor suppression through a lethal EMT [J] .Cell，2016，164(5)：1015-1030.
[16] Oshimori N，Oristian D，Fuchs E.TGF-β promotes heterogeneity and drug resistance in squamous cell carcinoma [J] .Cell，2015，160(5)：963-976.
[17] Neuzillet C，Tijeras-Raballand A，Cohen R，et al.Targeting the TGFβ pathway for cancer therapy [J] .Pharmacology & Therapeutics，2015，147(01)：22-31.
[18] Morikawa M，Derynck R，Miyazono K.TGF-β and the TGF-β family：Context-dependent roles in cell and tissue physiology [J] .Cold Spring Harbor Perspectives in Biology，2016，8(5)：a021873.
[19] Narimatsu M，Samavarchi-Tehrani P，Varelas X，et al.Distinct polarity cues direct Taz/Yap and TGFβ receptor localization to differentially control TGFβ-induced Smad signaling [J] .Developmental Cell，2015，32(5)：652-656.
[20] Wu M，Chen G，Li YP.TGF-β and BMP signaling in osteoblast，skeletal development，and bone formation，homeostasis and disease [J] .Bone Research，2016，4(41)：16009.

备注/Memo: 四川省卫生和计划生育委员会支助项目（编号：J201800103）

更新日期/Last Update: 1900-01-01