



期刊导读

6卷14期 2012年7月 [最新]



期刊存档

[查看目录](#)

期刊订阅



在线订阅



邮件订阅



RSS

作者中心



晋升信息



作者查稿



写作技巧



投稿方式



作者指南



期刊服务



建议我们



会员服务



广告合作



继续教育

您的位置: [首页](#)>> 文章摘要

PI3K/Akt信号传导通路与肿瘤多药耐药研究进展

张晔, 刘云鹏

张晔、刘云鹏，辽宁沈阳 中国医科大学附属第一医院肿瘤内科，110001

基金项目：国家自然科学基金青年基金(30901736)；辽宁省教育厅资助科研项目(L2010641)

摘要：磷脂酰肌醇3-激酶/蛋白激酶B[phosphatidylinositol-3-kinase(PI3K)/protein kinase B(Akt)]为细胞生存重要通路之一，在促进细胞生长、增殖，促进细胞运动、侵袭，抑制细胞凋亡，促进血管生成，抵抗凋亡作用。近年来，关于PI3K/Akt信号通路与药物耐药性关系的研究越来越多，并被认为是化疗耐药治疗的新靶点。Akt是PI3K的下游效应分子，多种肿瘤组织中都有Akt的过度表达和活化。多项实验表明，化疗药物可增加Akt磷酸化水平，但深入研究其作用机制，可能为肿瘤的基因治疗、抗肿瘤药物开发提供新靶点。

关键词：肿瘤

[评论](#) [收藏](#)

文献标引: 张晔, 刘云鹏. PI3K/Akt信号传导通路与肿瘤多药耐药研究进展[J/CD]. 中华临床医师杂志: 电子版, 2012, 6(14).

[复制](#)

参考文献:

- [1] Lane D, Robert V, Grondin R, et al. Malignant ascites protect against TRAIL-induced apoptosis by activating the PI3K/Akt pathway in human ovarian carcinoma cells. *Int J Cancer*, 2007, 120(1): 15-21. [\[PubMed\]](#)
- [2] Chen Y, Wang Z, Chang P, et al. The effect of focal adhesion kinase gene silencing on chemosensitivity involves an Akt/NF-kappaB signaling pathway in colorectal carcinoma cells. *Cancer*, 2010, 127(1): 195-206. [\[PubMed\]](#)
- [3] Gao X, Deeb D, Jiang H, et al. Synthetic triterpenoids inhibit growth and induce apoptosis in glioblastoma and neuroblastoma cells through inhibition of prosurvival Akt, NF-kappaB, and ERK signaling. *J Neurooncol*, 2007, 84(2): 147-157. [\[PubMed\]](#)
- [4] Dan HC, Baldwin AS. Differential involvement of IkappaB kinases alpha and beta in insulin-induced mammalian target of rapamycin activation determined by Akt. *J Immunol*, 2005, 175(10): 7582-7589. [\[PubMed\]](#)
- [5] Ripka S, Neesse A, Riedel J, et al. CUX1: target of Akt signalling and mediator of apoptosis in pancreatic cancer. *Gut*, 2010, 59(8): 1101-1110. [\[PubMed\]](#)
- [6] Lim WT, Zhang WH, Miller CR, et al. PTEN and phosphorylated AKT expression in early-and late-stage non-small cell lung cancer. *Oncol Rep*, 2007, 17(4): 853-857. [\[PubMed\]](#)
- [7] Zhang H, Bajraszewski N, Wu E, et al. PDGFRs are critical for PI3K/Akt activation and mTOR phosphorylation in non-small cell lung cancer. *J Clin Invest*, 2007, 117(3): 730-738. [\[PubMed\]](#)
- [8] Kumar N, Afeyan R, Sheppard S, et al. Quantitative analysis of Akt phosphorylation response to EGF and insulin treatment. *Biochem Biophys Res Commun*, 2007, 354(1): 14-20. [\[PubMed\]](#)

- [9] Cao H, Dronadula N, Rao GN. Thrombin induces expression of FGF-2 via activation of PI3K/Akt signaling axis leading to DNA synthesis and motility in vascular smooth muscle cells. *J Physiol*, 2006, 580(1): C172–182. [\[PubMed\]](#)
- [10] Yang CM, Lin MI, Hsieh HL, et al. Bradykinin-induced p42/p44 MAPK phosphorylation and proliferation via Src, EGF receptors, and PI3K-Akt in vascular smooth muscle cells. *J Physiol*, 2005, 573(3): 538–546. [\[PubMed\]](#)
- [11] Badr G, Saad H, Waly H, et al. Type I interferon(IFN-alpha/beta) rescues B-lymphoma cells from apoptosis via PI3Kdelta/Akt, Rho-A, NFkappaB and Bcl-2/Bcl(XL). *Cell Immunol*, 2010, 266(1): 1–8. [\[PubMed\]](#)
- [12] Basso AD, Solit DB, Munster PN, et al. Ansamycin antibiotics inhibit Akt activation and expression in breast cancer cells that overexpress HER2. *Oncogene*, 2002, 21(8): 1159–1167. [\[PubMed\]](#)
- [13] Sunters A, Madureira PA, Pomeranz KM, et al. Paclitaxel-induced nuclear translocation of Akt in breast cancer cells is mediated by c-Jun NH₂-terminal kinase and Akt. *Cancer Res*, 2004, 64(18): 6631–6638. [\[PubMed\]](#)
- [14] Gagnon V, St-Germain ME, Parent S, et al. Akt activity in endometrial cancer promotes cell survival through cIAP-1. *Int J Oncol*, 2003, 23(3): 803–810. [\[PubMed\]](#)
- [15] Johnson NC, Dan HC, Cheng JQ, et al. BRCA1 185delAG mutation inhibits Akt-dependent caspase 3 inactivation in human ovarian surface epithelial cells. *Exp Cell Res*, 2004, 295(1): 10–17. [\[PubMed\]](#)
- [16] Zhao P, Meng Q, Liu LZ, et al. Regulation of survivin by PI3K/Akt/p70S6K1 pathway. *Res Commun*, 2010, 395(2): 219–224. [\[PubMed\]](#)
- [17] Duguay D, deBlois D. Differential regulation of Akt, caspases and MAP kinases in vascular smooth muscle cell apoptosis during aortic remodelling in SHR treated with amlodipine. *Br J Pharmacol*, 2008, 153(8): 1315–1323. [\[PubMed\]](#)
- [18] Babchuk N, Calipel A, Mouriaux F, et al. The PI3K/Akt and mTOR/P70S6K signaling pathways in uveal melanoma cells: interaction with B-Raf/ERK. *Invest Ophthalmol Vis Sci*, 2010, 51(10): 6631–6638. [\[PubMed\]](#)
- [19] Presneau N, Shalaby A, Idowu B, et al. Potential therapeutic targets for chordoma: PI3K/AKT/TSC1/TSC2/mTOR pathway. *Br J Cancer*, 2009, 100(9): 1406–1414. [\[PubMed\]](#)
- [20] Wu X, Reiter CE, Antonetti DA, et al. Insulin promotes rat retinal neuronal cell survival in a p70S6K-dependent manner. *J Biol Chem*, 2004, 279(10): 9167–9175. [\[PubMed\]](#)
- [21] Wang L, Cao XX, Chen Q, et al. DIXDC1 targets p21 and cyclin D1 via PI3K pathway to promote colon cancer cell proliferation. *Cancer Sci*, 2009, 100(10): 1801–1808. [\[PubMed\]](#)
- [22] Peltier J, O' Neill A, Schaffer DV. PI3K/Akt and CREB regulate adult neural stem cell proliferation and differentiation. *Dev Neurobiol*, 2007, 67(10): 1348–1361. [\[PubMed\]](#)
- [23] Garat CV, Fankell D, Erickson PF, et al. Platelet-derived growth factor BB induces the phosphorylation and proteasomal degradation of CREB via phosphatidylinositol 3-kinase/Akt signaling in vascular smooth muscle cells. *Mol Cell Biol*, 2006, 26(13): 4934–4948. [\[PubMed\]](#)
- [24] Feng Z, Hu W, de Stanchina E, et al. The regulation of AMPK beta1, TSC2, and PI3K/Akt/p53: stress, cell and tissue specificity, and the role of these gene products in mTOR signaling. *Cancer Res*, 2007, 67(7): 3043–3053. [\[PubMed\]](#)
- [25] Kim CS, Vasko VV, Kato Y, et al. AKT activation promotes metastasis in a mouse model of thyroid carcinoma. *Endocrinology*, 2005, 146(10): 4456–4463. [\[PubMed\]](#)
- [26] Liang Z, Brooks J, Willard M, et al. CXCR4/CXCL12 axis promotes VEGF-mediated angiogenesis through Akt signaling pathway. *Biochem Biophys Res Commun*, 2007, 359(3): 716–722. [\[PubMed\]](#)
- [27] Gao N, Nester RA, Sarkar MA. 4-Hydroxy estradiol but not 2-hydroxy estradiol increases hypoxia-inducible factor 1alpha and vascular endothelial growth factor A through phosphatidylinositol 3-kinase/Akt/FRAP pathway in OVCAR-3 and A2780-CP70 human ovarian carcinoma cells. *Toxicol Pharmacol*, 2004, 196(1): 124–135. [\[PubMed\]](#)
- [28] Huang Y, Hua K, Zhou X, et al. Activation of the PI3K/AKT pathway mediates FSH_β expression in ovarian serous cystadenocarcinoma. *Cell Res*, 2008, 18(7): 780–791. [\[PubMed\]](#)
- [29] Michl P, Downward J. Mechanisms of disease: PI3K/AKT signaling in gastrointestinal cancer. *Gastroenterol*, 2005, 133(10): 1133–1139. [\[PubMed\]](#)
- [30] Han Z, Hong L, Han Y, et al. Phospho Akt mediates multidrug resistance of gastric cancer cells through regulation of P-gp, Bcl-2 and Bax. *J Exp Clin Cancer Res*, 2007, 26(2): 261–268. [\[PubMed\]](#)

- [31] Oki E, Baba H, et al. Akt phosphorylation associates with LOH of PTEN and chemoresistance for gastric cancer. *Int J Cancer*, 2005, 117(3): 376–380. [\[PubMed\]](#)
- [32] Yuan ZQ, Feldman RI, Sussman GE, et al. AKT2 inhibition of cisplatin-induced JNK activation by phosphorylation of ASK1: implication of AKT2 in chemoresistance. *J Biol Chem*, 2006, 281(26): 23432–23440. [\[PubMed\]](#)
- [33] Jin W, Wu L, Liang K, et al. Roles of the PI-3K and MEK pathways in Ras-mediated transformation of breast cancer cells. *Br J Cancer*, 2003, 89(1): 185–191. [\[PubMed\]](#)
- [34] Simon PO Jr, McDunn JE, Kashiwagi H, et al. Targeting AKT with the proapoptotic compound PP242: a novel strategy for the treatment of human pancreatic adenocarcinoma. *Int J Cancer*, 2005, 115(5): 1033–1040. [\[PubMed\]](#)
- [35] Zhang Y, Qu X, Hu X, et al. Reversal of P-glycoprotein-mediated multi-drug resistance by Cbl-b in human gastric adenocarcinoma cells. *J Pathol*, 2009, 218(2): 160–167. [\[PubMed\]](#)
- [36] O'Gorman DM, McKenna SL, McGahon AJ, et al. Inhibition of PI3-kinase sensitizes leukaemia cells to both chemotherapeutic drug- and Fas-induced apoptosis by a JNK independent pathway. *Leuk Res*, 2001, 25(9): 801–811. [\[PubMed\]](#)
- [37] Jazirehi AR, Vega MI, Chatterjee D, et al. Inhibition of the Raf-MEK1/2-ERK1/2-Bcl-xL down-regulation, and chemosensitization of non-Hodgkin's lymphoma B cells by LY294002. *Cancer Res*, 2004, 64(19): 7117–7126. [\[PubMed\]](#)
- [38] Jiang H, Fan D, Zhou G, et al. Phosphatidylinositol 3-kinase inhibitor (LY294002) induces apoptosis of human nasopharyngeal carcinoma in vitro and in vivo. *J Exp Clin Cancer Res*, 2005, 24(1): 1–7. [\[PubMed\]](#)
- [39] Lane D, Robert V, Grondin R, et al. Malignant ascites protect against TRAIL-induced apoptosis by activating the PI3K/Akt pathway in human ovarian carcinoma cells. *Int J Cancer*, 2007, 117(10): 2267–2274. [\[PubMed\]](#)
- [40] Ogata Y, Osaki T, Naka T, et al. Overexpression of PIAS3 suppresses cell growth and drug sensitivity of human lung cancer cells in association with PI3-K/Akt inactivation. *Cancer Lett*, 2005, 221(10): 817–825. [\[PubMed\]](#)

综述

耳廓假性囊肿的研究进展

马桂琴, 李连贺. . 中华临床医师杂志: 电子版
2011;5(2):435-437.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

乳腺癌常规治疗失败后的替代药物

陈振东, 程怀东. . 中华临床医师杂志: 电子版
2011;5(2):438-441.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

stomatin家族与恶性肿瘤

常栎, 王天佑, 刘芝华. . 中华临床医师杂志: 电子版
2011;5(2):442-445.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

PI3K/Akt信号传导通路与肿瘤多药耐药研究进展

张晔, 刘云鹏. . 中华临床医师杂志: 电子版
2011;5(2):446-449.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

腹腔镜在小儿外科的应用及进展

张强业, 张刚, 李爱武. . 中华临床医师杂志: 电子版
2011;5(2):450-453.

内毒素血症的免疫学发病机制

郭媛, 魏筱华, 谢珺, 白爱平. . 中华临床医师杂志: 电子版
2011;5(2):454-456.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

炎症因子与慢性心力衰竭

何文俊, 张涛, 蒋学俊, 林洪平. . 中华临床医师杂志: 电子版
2011;5(2):457-460.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

脂肪源性干细胞的定向分化潜能及临床应用前景

王伟, 撒亚莲, 严新民. . 中华临床医师杂志: 电子版
2011;5(2):461-464.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

内脂素与妊娠期糖尿病关系的研究进展

刘斌, 王子莲. . 中华临床医师杂志: 电子版
2011;5(2):465-468.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)

肝脏转氨酶升高对预测患者临床转归的意义

郑刚. . 中华临床医师杂志: 电子版
2011;5(2):469-472.

[摘要](#) [FullText](#) | [PDF](#) | [评论](#) | [收藏](#)