



中华临床医师杂志

(电子版)
Chinese Journal of Clinicians (Electronic Edition)

登

[期刊导读](#)

9卷14期 2015年7月 [最新]

[期刊存档](#)

[期刊存档](#) [查看目录](#)

[期刊订阅](#)

[在线订阅](#)

[邮件订阅](#)

[RSS](#)

[资质及晋升信息](#)

[作者查稿](#)

[写作技巧](#)

[投稿方式](#)

[作者指南](#)

编委会

[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[中文](#)[English](#)

Nrf2信号通路在各系统肿瘤中的研究进展

郑文键, 张协军, 黄国栋

515041 广东省, 汕头大学医学院(郑文键、黄国栋); 深圳大学第一附属医院(深圳市第二人民医院)神经外科(黄国栋)

黄国栋, Email: jxgd211@163.com

摘要:活性氧自由基(ROS)可以损伤细胞DNA和蛋白质,具有致癌作用。Nrf2可以激活人体内多种基因表达,其活性主要由Keap1负性调节,当机体受到外界药物、射线等刺激时,Nrf2可激活ARE区域,介导细胞保护的作用,目前已有部分研究表明某些植物与药物通过Nrf2信号通路发挥抗癌作用。近期,有学者发现Nrf2同样具有致癌作用,肿瘤细胞通过Nrf2或Keap1突变与基因杂合性丢失,使Nrf2和Keap1蛋白在胞内积累,激活下游基因,增加肿瘤细胞内的解毒酶,从而增强细胞对放化疗的抵抗性。人体的大部分消化系统、呼吸系统、生殖系统及神经系统肿瘤中均呈高表达,并与多种致癌基因Raf、Myc、BRCA1等基因表达相关,阻断Nrf2信号通路的抗癌药物研究已表明其能够减少肿瘤复发和治疗药物的敏感性。Nrf2参与着各个系统众多肿瘤的发生与发展,将成为未来肿瘤靶向治疗的重点。

关键词:氧化性应激; 抗药性, 肿瘤; 肿瘤, 实验性; 肿瘤标记, 生物学; NF-E2相关因子2

[评论](#) [收藏](#) [全文](#)

文献标引: 郑文键, 张协军, 黄国栋. Nrf2信号通路在各系统肿瘤中的研究进展[J/CD]. 中华临床医师杂志: 电子版, 3524. [复制](#)

参考文献:

- [1] Zhang M, An C, Gao Y, et al. Emerging roles of Nrf2 and phase II antioxidant enzymes in neuroprotection[J]. Progress in Neurobiology, 2013, 100: 30-47.
- [2] Bryan HK, Olayanju A, Goldring CE, et al. The Nrf2 cell defence pathway: Keap1-independent mechanisms of regulation[J]. Biochem Pharmacol, 2013, 85(6): 705-717.
- [3] Du Y, Villeneuve NF, Wang XJ, et al. Oridonin confers protection against arsenite toxicity through activation of the Nrf2-mediated defensive response[J]. Environ Health Perspect, 2009, 116(9): 1154-1161.
- [4] Ray PD, Huang BW, Tsuji Y. Reactive oxygen species (ROS) homeostasis and redox cellular signaling[J]. Cell Signal, 2012, 24(5): 981-990.
- [5] Rotblat B, Melino G, Knight RA. NRF2 and p53: Januses in cancer?[J]. Oncotarget, 2015, 6(3): 1830-1842.

- [6] Delgado-Buenrostro NL, Medina-Reyes EI, Lastres-Becker I, et al. Nrf2 protects against inflammation induced by titanium dioxide nanoparticles: A positive regulator role of Nrf2 release[J]. Environ Toxicol, 2014.
- [7] Leonardo CC, Agrawal M, Singh N, et al. Oral administration of the flavanol catechins bolsters endogenous protection against focal ischemia through the Nrf2 cytoprotective pathway[J]. Neurosci, 2013, 38(11): 3659–3668.
- [8] Taguchi K, Motohashi H, Yamamoto M. Molecular mechanisms of the Keap1-Nrf2 pathway in response and cancer evolution[J]. Genes Cells, 2011, 16(2): 123–140.
- [9] Kalthoff S, Ehmer U, Freiberg N, et al. Coffee induces expression of glucuronyl transferase, the aryl hydrocarbon receptor and Nrf2 in liver and stomach[J]. Gastroenterology, 2008, 135(10): 1710, e1–e2.
- [10] Shibuya A, Onda K, Kawahara H, et al. Sofalcone, a gastric mucosa protective agent, increases vascular endothelial growth factor via the Nrf2-heme-oxygenase-1 dependent pathway in intestinal epithelial cells[J]. Biochem Biophys Res Commun, 2010, 398(3): 581–584.
- [11] 汤晓飞, 赵艳华, 张教, 等. Nrf2和NF- κ B在口腔癌和癌前病变细胞中的表达及意义[J]. 中国口腔医学研究杂志, 2009, 17(3): 135–137.
- [12] 耿苗, 唐修文. Nrf2-ARE信号通路与胃癌耐药关系的研究进展[J]. 中国细胞生物学学报, 2010, 22(11): 1129–1133.
- [13] 陈浩许. Nrf2_NQO1信号通路在胃癌干细胞氧化应激反应中的作用机制[J]. 吉林大学学报(医学版), 2010, 39(3): 463–466.
- [14] Niture SK, Jaiswal AK. Nrf2 protein up-regulates antiapoptotic protein Bcl-2 and inhibits cellular apoptosis[J]. J Biol Chem, 2012, 287(13): 9873–9886.
- [15] Akhdar H, Loyer P, Rauch C, et al. Involvement of Nrf2 activation in resistance to 5-fluorouracil in human colon cancer HT-29 cells[J]. Eur J Cancer, 2009, 45(12): 2219–2226.
- [16] Stacy DR, Ely K, Massion PP, et al. Increased expression of nuclear factor (NF)- κ B and nuclear factor 2 (NRF2) in head and neck squamous cell carcinomas[J]. Head Neck, 2006, 28(9): 1111–1117.
- [17] 毛景涛, 叶尔买克?唐沙哈尔, 沈辉, 等. Nrf2在食管鳞癌组织中的表达及意义[J]. 维吾尔族医药, 2011, 27(11): 1231–1233.
- [18] Yoo NJ, Kim YR, Lee SH. Expression of NRF2, a cytoprotective protein, in gastric adenocarcinoma cells[J]. Apmis, 2010, 118(8): 613–614.
- [19] 杨海明, 张明鑫, 王健生, 等. 原发性胆囊癌中Nrf2的表达及意义[J]. 现代肿瘤医学, 2010, 28(7): 747.
- [20] Ji L, Wei Y, Jiang T, et al. Correlation of Nrf2, NQO1, MRP1, cmyc and p53 with clinicopathologic features and survival in gallbladder carcinoma[J]. Int J Clin Exp Pathol, 2010, 3(3): 1124–1131.
- [21] Malkinson AM. Molecular comparison of human and mouse pulmonary adenocarcinoma[J]. J Cell Physiol, 2000, 183(2): 187–194.

- [22] DeNicola GM, Karreth FA, Humpton TJ, et al. Oncogene-induced Nrf2 transcriptional detoxification and tumorigenesis[J]. *Nature*, 2011, 475(7354): 106–109.
- [23] Singh A, Boldin-Adamsky S, Thimmulappa RK, et al. RNAi-mediated silencing of erythroid-2-related factor 2 gene expression in non-small cell lung cancer inhibits increases efficacy of chemotherapy[J]. *Cancer Res*, 2008, 68(19): 7975–7984.
- [24] Solis LM, Behrens C, Dong W, et al. Nrf2 and Keap1 abnormalities in non-small cell carcinoma and association with clinicopathologic features[J]. *Clin Cancer Res*, 2010, 16(10): 2700–2707.
- [25] Lee S, Lim MJ, Kim MH, et al. An effective strategy for increasing the radiosensitivity of Human lung Cancer cells by blocking Nrf2-dependent antioxidant responses[J]. *Free Radic Biol Med*, 2007, 53(4): 807–816.
- [26] Ren D, Villeneuve NF, Jiang T, et al. Brusatol enhances the efficacy of chemotherapy by inhibiting the Nrf2-mediated defense mechanism[J]. *Proc Natl Acad Sci U S A*, 2011, 108(40): 16636–16641.
- [27] Wang Q, Li J, Yang X, et al. Nrf2 is associated with the regulation of basal transcriptional activity of the BRCA1 gene[J]. *Acta Biochim Biophys Sin (Shanghai)*, 2013, 45(3): 179–186.
- [28] Zhong Y, Zhang F, Sun Z, et al. Drug resistance associates with activation of Nrf2 in ovarian cancer cells, wogonin reverses it by down-regulating Nrf2-mediated cellular defense responses[J]. *Cancer Lett*, 2013, 52(10): 824–834.
- [29] Zhang Z, Wang Q, Ma J, et al. Reactive oxygen species regulate FSH-induced proliferation of vascular endothelial growth factor via Nrf2 and HIF1alpha signaling in human epithelial ovarian cancer[J]. *Oncol Rep*, 2013, 29(4): 1429–1434.
- [30] Cho JM, Manandhar S, Lee HR, et al. Role of the Nrf2-antioxidant system in cisplatin-induced apoptosis mediated by anticancer cisplatin: implication to cancer cell resistance[J]. *Cancer Lett*, 2013, 329(1): 96–108.
- [31] Wu YJ, Neuwelt AJ, Muldoon LL, et al. Acetaminophen enhances cisplatin- and carboplatin-induced cytotoxicity to SKOV3 human ovarian carcinoma[J]. *Anticancer Res*, 2013, 33(6): 2391–2396.
- [32] Jiang T, Chen N, Zhao F, et al. High levels of Nrf2 determine chemoresistance to cisplatin in endometrial cancer[J]. *Cancer Res*, 2010, 70(13): 5486–5496.
- [33] Hartikainen JM, Tengstrom M, Kosma VM, et al. Genetic polymorphisms and protein expression of NRF2 and Sulfiredoxin predict survival outcomes in breast cancer[J]. *Cancer Res*, 2011, 71(22): 5546–5553.
- [34] Onodera Y, Motohashi H, Takagi K, et al. NRF2 immunolocalization in human breast cancer patients as a prognostic factor[J]. *Endocr Relat Cancer*, 2014, 21(2): 241–252.
- [35] Liao H, Zhou Q, Zhang Z, et al. NRF2 is overexpressed in ovarian epithelial carcinoma and regulated by gonadotrophin and sex-steroid hormones[J]. *Oncol Rep*, 2012, 27(6): 1918–1925.
- [36] Chen N, Yi X, Abushahin N, et al. Nrf2 expression in endometrial serous carcinoma and its precancers[J]. *Int J Clin Exp Pathol*, 2010, 4(1): 85–96.

[37] Habas A, Hahn J, Wang X, et al. Neuronal activity regulates astrocytic Nrf2. *Natl Acad Sci U S A*, 2013, 110(45): 18291–18296.

[38] Lee JM, Shih AY, Murphy TH, et al. NF-E2-related factor-2 mediates neuroprotective effects of mitochondrial complex I inhibitors and increased concentrations of intracellular calcium in cortical neurons[J]. *J Biol Chem*, 2003, 278(39): 37948–37956.

[39] Zhang M, Wang S, Mao L, et al. Omega-3 fatty acids protect the brain against activating Nrf2 and upregulating heme oxygenase 1[J]. *J Neurosci*, 2014, 34(5): 1903–1913.

[40] Lastres-Becker I, Innamorato NG, Jaworski T, et al. Fractalkine activates Nrf2/heme oxygenase 1 to restrain tauopathy-induced microgliosis[J]. *Brain*, 2014, 137(Pt 1): 722–735.

[41] Cong ZX, Wang HD, Wang JW, et al. ERK and PI3K signaling cascades induce Nrf2-mediated cell viability partly through Nrf2 in human glioblastoma cells[J]. *Oncol Res*, 2012, 22(10): 722.

[42] Pan H, Wang H, Zhu L, et al. The involvement of Nrf2-ARE pathway in regulating proliferation and migration of human glioblastoma cell U251[J]. *Neurol Res*, 2013, 35(1): 71–78.

[43] Ji X, Wang H, Zhu J, et al. Correlation of Nrf2 and HIF-1alpha in glioblastoma: relationships to clinicopathologic features and survival[J]. *Neurol Res*, 2013, 35(10): 1057–1060.

[44] 林晓, 林青, 唐俐, 等. 髓母细胞瘤中PI3K、AKT及Nrf2的表达及其意义[J]. 中国生物医学工程学杂志, 2013, 24(9): 1057–1060.

综述

内皮间质转化在糖尿病大血管病变中的作用

王瑞风, 杜宏. . 中华临床医师杂志: 电子版

2014;8(19):3508–3511.

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

探讨Cycloset治疗2型糖尿病的临床前景

何亮军, 谢作玲. . 中华临床医师杂志: 电子版

2014;8(19):3512–3515.

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

甲状腺功能减退症的非手术治疗进展

陈佳, 霍景山. . 中华临床医师杂志: 电子版

2014;8(19):3516–3519.

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

Nrf2信号通路在各系统肿瘤中的研究进展

郑文键, 张协军, 黄国栋. . 中华临床医师杂志: 电子版

2014;8(19):3520–3524.

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

脓毒症线粒体损伤研究进展

李宁, 张琪. . 中华临床医师杂志: 电子版

2014;8(19):3525–3530.

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

谷氨酰胺对肝缺血/再灌注后肺损伤保护作用的研究进展

刘荣, 罗振中. . 中华临床医师杂志: 电子版
2014;8(19):3531-3533.

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

seladin-1在阿尔茨海默病中的保护作用及其机制

张鑫, 赵乃倩, 刘晓玲, 段再康. . 中华临床医师杂志: 电子版
2014;8(19):3534-3540.

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

脑瘫患儿髋关节脱位康复治疗的研究进展

黄晶晶, 周云, 吴建贤. . 中华临床医师杂志: 电子版
2014;8(19):3541-3546.

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

小儿先天性二尖瓣畸形的外科治疗进展

曹芳, 莫绪明. . 中华临床医师杂志: 电子版
2014;8(19):3547-3552.

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

| 编委会 | 联系我们 | 合作伙伴 | 友情链接 |

© 2015版权声明 中华临床医师杂志(电子版)编辑部
网站建设: 北京华夏世通信息技术有限公司 京ICP备0
北京市公安局西城分局备案编号: 110102000676