

# 自噬在恶性肿瘤治疗中的进展及影像学应用前景

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**Title:** The progress of autophagy in the treatment of malignant tumors and imaging applications

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**摘要:** 自噬是在营养缺乏条件下维持细胞代谢的主要途径。这使其成为肿瘤研究的新热点, 调控自噬信号通路的机制已经很明确, 越来越多的研究发现机体细胞自噬活性变化对肿瘤治疗的效果具有巨大影响。但缺乏能够重复比较或靶向定位自噬活性的测量技术。正电子示踪剂PET等影像手段通过将相关自噬的信号通路蛋白标记放射性核素进行显像似乎具有解决这些问题的潜力。在本文中, 我们综述自噬在肿瘤治疗中的应用, 并展望医学影像技术协助自噬治疗肿瘤的前景。

**Abstract:** Autophagy is the main way to maintain cell metabolism under nutrient deficiencies. This has made it a new hot spot in cancer research. The mechanism of regulating autophagy signaling pathway has been very clear. More and more studies have found that the change of autophagic activity of the cell body has a great influence on the curative effect of anti-tumor therapy. However, there is a lack of measurement technology that can repeatedly compare or target the localization of autophagy activity. Positron-tracer imaging tools such as PET appear to have the potential to solve these problems by visualizing relevant autophagic signaling protein labeled radionuclides. In this article, we review the use of autophagy in cancer therapy. Finally, we look to the future of medical imaging techniques to assist autophagy in the treatment of tumors.

## 参考文献/REFERENCES

- [1] Shing Y, Vincent W, Cheung W, et al. Influence of autophagy on the efficacy of radiotherapy [J]. *Radiat Oncol*, 2017, 12(1): 57.
- [2] Galluzzi L, Pietrocola F, BravoSan Pedro JM, et al. Autophagy in malignant transformation and cancer progression [J]. *Embo Journal*, 2015, 34(7): 856-880.
- [3] Gewirtz DA. Autophagy, senescence and tumor dormancy in cancer therapy [J]. *Autophagy*, 2009, 5(8): 1232-1234.
- [4] Li J, Hou N, Faried A, et al. Inhibition of autophagy augments 5-fluorouracil chemotherapy in human colon cancer in vitro and in vivo model [J]. *European Journal of Cancer*, 2010, 46(10): 1900-1909.
- [5] Zhao XG, Sun RJ, Yang XY, et al. Chloroquine-enhanced efficacy of cisplatin in the treatment of hypopharyngeal carcinoma in xenograft mice [J]. *PLoS One*, 2015, 10(4): e0126147.
- [6] Golden EB, Cho HY, Jahanian A, et al. Chloroquine enhances temozolomide cytotoxicity in malignant gliomas by blocking autophagy [J]. *Neurosurgical Focus*, 2014, 37(6): E12.
- [7] Pan Y, Gao Y, Chen L, et al. Targeting autophagy augments in vitro and in vivo antimyeloma activity of DNA-damaging chemotherapy [J]. *Clinical Cancer Research*, 2011, 17(10): 3248.
- [8] Chittaranjan S, Bortnik S, Dragowska WH, et al. Autophagy inhibition augments the anticancer effects of epirubicin treatment in anthracycline-sensitive and-resistant triple-negative breast cancer [J]. *Clin Cancer Res*, 2014, 20: 3159-3173.
- [9] Lefort S, Joffre C, Kieffer Y, et al. Inhibition of autophagy as a new means of improving chemotherapy efficiency in high-LC3B triple-negative breast cancers [J]. *Autophagy*, 2014, 10:2122-2142.
- [10] Dragowska WH, Weppeler SA, Wang JC, et al. Induction of autophagy is an early response to gefitinib and a potential therapeutic target in breast cancer [J]. *PLoS One*, 2013, 8: e76503.
- [11] Zhao Xiangxuan, Ren Ying, Wen Feng, et al. Role of autophagy in sorafenib-induced apoptosis of

- hepatoma cells [J]. *Modern Oncology*, 2016, 24(10): 1505-1508. [赵相轩, 任莹, 温峰, 等.自噬在索拉菲尼诱导肝癌细胞凋亡中的作用 [J].现代肿瘤医学, 2016, 24(10): 1505-1508.]
- [12] Nguyen HG, Yang JC, Kung HJ, et al. Targeting autophagy overcomes enzalutamide resistance in castration-resistant prostate cancer cells and improves therapeutic response in a xenograft model [J]. *Oncogene*, 2014, 33(36):4521-4530.
- [13] Selvakumaran M, Amaravadi RK, Vasilevskaya IA, et al. Inhibition sensitizes colon cancer cells to antiangiogenic and cytotoxic therapy [J]. *Clinical Cancer Research An Official Journal of the American Association for Cancer Research*, 2013, 19:2995-3007.
- [14] Lin J, Huang Z, Wu H, et al. Inhibition of autophagy enhances the anticancer activity of silver nanoparticles [J]. *Autophagy*, 2014, 10:2006-2020.
- [15] Tseng HC, Liu WS, Tyan YS, et al. Sensitizing effect of 3-methyladenine on radiation-induced cytotoxicity in radio-resistant HepG2 cells in vitro and in tumor xenografts [J]. *Chem Biol Interact*, 2011, 192:201-208.
- [16] Wolpin BM, Rubinson DA, Wang X, et al. Phase II and pharmacodynamic study of autophagy inhibition using hydroxychloroquine in patients with metastatic pancreatic adenocarcinoma [J]. *Oncologist*, 2014, 19:637-638.
- [17] Kimura T, Takabatake Y, Takahashi A, et al. Chloroquine in cancertherapy: A double-edged sword of autophagy [J]. *Cancer Res*, 2013, 73(1): 3-7.
- [18] Rangwala R, Leone R, Chang YC, et al. Phase I trial of hydroxychloroquine with dose-intense temozolomide in patients with advanced solid tumors and melanoma [J]. *Autophagy*, 2014, 10:1369-1379.
- [19] Rojas-Puentes LL, Gonzalez-Pinedo M, Crismatt A, et al. Phase II randomized, double-blind, placebo-controlled study of whole-brain irradiation with concomitant chloroquine for brain metastases [J]. *Radiat Oncol*, 2013, 8(1): 209.
- [20] Piconi S, Parisotto S, Rizzardini G, et al. Hydroxychloroquine drastically reduces immune activation in HIV-infected, antiretroviral therapy-treated immunologic nonresponders [J]. *Blood*, 2011, 118(12): 3263-3272.
- [21] Maes H, Kuchnio A, Peric A, et al. Tumor vessel normalization by chloroquine independent of autophagy [J]. *Cancer Cell*, 2014, 26(2): 190.
- [22] Lan YY, Londoño D, Bouley R, et al. Dnase2a deficiency uncovers lysosomal clearance of damaged nuclear DNA via autophagy [J]. *Cell Reports*, 2014, 9(1): 180-192.
- [23] Galluzzi L, Buqué A, Kepp O, et al. Immunological effects of conventional chemotherapy and targeted anticancer agents [J]. *Cancer Cell*, 2015, 28(6): 690-714.
- [24] Ma Y, Adjeman S, Mattarollo SR, et al. Anticancer chemotherapy-induced intratumoral recruitment and differentiation of antigen-presenting cells [J]. *Immunity*, 2013, 38(4): 729-741.
- [25] Galluzzi L, Bravo-San Pedro JM, Demaria S, et al. Activating autophagy to potentiate immunogenic chemotherapy and radiation therapy [J]. *Nature Reviews Clinical Oncology*, 2017, 14(4): 247.
- [26] Pietrocola F, Pol J, Vacchelli E, et al. Caloric restriction mimetics enhance anticancer immuno-surveillance [J]. *Cancer Cell*, 2016, 30(1): 147-160.
- [27] Ko A, Kanehisa A, Martins I, et al. Autophagy inhibition radiosensitizes in vitro, yet reduces radioresponses in vivo due to deficient immunogenic signalling [J]. *Cell Death & Differentiation*, 2014, 21(1): 92-99.
- [28] Sirichanchuen B, Pengsuparp T, Chanvorachote P. Long-term cisplatin exposure impairs autophagy and causes cisplatin resistance in human lung cancer cells [J]. *Molecular & Cellular Biochemistry*, 2012, 364(1-2): 11-18.
- [29] Palumbo S, Pirtoli L, Tini P, et al. Different involvement of autophagy in human malignant glioma cell lines undergoing irradiation and temozolomide combined treatments [J]. *Cell Biochem*, 2012, 113(7): 2308-2318.
- [30] Wu SY, Liu YW, Wang YK, et al. Ionizing radiation induces autophagy in human oral squamous cell carcinoma [J]. *J BUON*, 2014, 19(1): 137-144.
- [31] Paglin S, Lee NY, Nakar C, et al. Rapamycin-sensitive pathway regulates mitochondrial membrane potential, autophagy, and survival in irradiated MCF-7 cells [J]. *Cancer Res*, 2005, 65(23): 11061-11070.
- [32] Kim KW, Moretti L, Mitchell LR, et al. Combined Bcl-2/mammalian target of rapamycin inhibition leads to enhanced radiosensitization via induction of apoptosis and autophagy in non-small cell lung tumor xenograft model [J]. *Clin Cancer Res*, 2009, 15(19): 6096-6105.
- [33] Koukourakis MI, Kalamida D, Mitrikas A, et al. Intensified autophagy compromises the efficacy of radiotherapy against prostate cancer [J]. *Biochem Biophys Res Commun*, 2015, 461(2): 268-274.
- [34] Chiu HW, Lin SW, Lin LC, et al. Synergistic antitumor effects of radiation and proteasome inhibitor treatment in pancreatic cancer through the induction of autophagy and the downregulation of TRAF6 [J]. *Cancer Lett*, 2015, 365(2): 229-239.
- [35] Yang M, Zhao H, Guo L, et al. Autophagy-based survival prognosis in human colorectal carcinoma [J]. *Oncotarget*, 2015, 6(9): 7084.
- [36] Jung G, Roh J, Lee H, et al. Autophagic markers BECLIN 1 and LC3 are associated with prognosis of multiple myeloma [J]. *Acta Haematologica*, 2015, 134(1): 17.
- [37] Apetoh L, Ghiringhelli F, Tesniere A, et al. Toll-like receptor 4-dependent contribution of the immune system to anticancer chemotherapy and radiotherapy [J]. *Nat Med*, 2007, 13(9): 1050-1059.
- [38] Ladoire S, Penault-Llorca F, Senovilla L, et al. Combined evaluation of LC3B puncta and HMGB1

- expression predicts residual risk of relapse after adjuvant chemotherapy in breast cancer [J] .Autophagy, 2015, 11(10): 1878.
- [39] Pigna E, Berardi E, Aulino P, et al.Aerobic exercise and pharmacological treatments counteract cachexia by modulating autophagy in colon cancer [J] .Scientific Reports, 2016, 6: 26991.
- [40] Wang Rongfu.Research on the application of radioactive positron drugs in tumors [J] .Journal of Practical Oncology, 2006, 21(1): 92-95. [王荣福.放射性正电子药物在肿瘤中的应用研究 [J] .实用肿瘤杂志, 2006, 21(1): 92-95.]
- [41] Lakhani A, Khan SR, Bharwani N, et al.FDG PET/CT pitfalls in gynecologic and genitourinary oncologic imaging [J] .Radiographics, 2017, 37(2): 577-594.
- [42] Zhang Jing, Shu Lisha, Zhang Linxi.Expression and significance of autophagy-related genes BECN1, LC3B and mTOR in the progression of cervical squamous epitheliopathy [J] .Modern Obstetrics and Gynecology, 2017, 26(7): 497-501. [张晶, 舒丽莎, 张林西.自噬相关基因BECN1、LC3B、mTOR在宫颈鳞状上皮病变进展中的表达及意义 [J] .现代妇产科进展, 2017, 26(7): 497-501.]
- [43] Duan Changhu, Liu Xiaochen, Dou Fafu, et al.Relationship between HBx and Beclin1 expression in hepatocellular carcinoma [J] .Liver, 2017, 22(1): 20-23. [段昌虎, 刘晓晨, 豆发福, 等.HBx及Beclin1在肝癌中表达的关系研究 [J] .肝脏, 2017, 22(1): 20-23.]
- [44] Lou Xiaoyu.Diffusion-weighted imaging and clinical value of autophagy-related protein expression in cervical cancer [D] .Zhengzhou: Zhengzhou University, 2015. [娄晓宇.扩散加权成像及自噬相关蛋白表达在宫颈癌中的临床价值研究 [D] .郑州: 郑州大学, 2015.]

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