

# LOX家族在肿瘤中的研究进展

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**Title:** Progress in research of LOX family in tumor

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**关键词:** 赖氨酰氧化酶; 胶原合成; 肿瘤; 转移

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**摘要:** 赖氨酰氧化酶 (LOX) 家族是一组细胞外铜依赖性胺氧化酶, 主要作用是共价交联胶原蛋白和弹性蛋白, 维持细胞外基质的正常结构和功能。近年来的研究显示, LOX还可通过促进上皮-间质转化 (EMT)、激活FAK信号通路、参与转移前微环境形成等促进肿瘤细胞迁移和侵袭, 在肿瘤的发生发展及转移等过程中具有重要的作用, 有望成为肿瘤治疗的潜在靶点。本文拟从LOX家族的结构与调控、在肿瘤中的表达及作用机制等方面进行综述, 以全面了解LOX家族的研究现状。

**Abstract:** The lysyl oxidase (LOX) family is a group of extracellular copper-dependent amine oxidases. The main role of LOX family is covalently cross-linking collagen and elastin and maintaining the normal structure and function of extracellular matrix. Recent studies have shown that LOX can also promote migration and invasion of tumor cells by promoting EMT, activating FAK signaling pathways, and participating in the formation of pre-metastatic microenvironment. It plays an important role in the development and metastasis of tumors and is expected to become a potential target for cancer treatment. This article intends to review the structure and regulation of the LOX family, its expression in tumors and its mechanism in order to fully understand the research status of the LOX family.

## 参考文献/REFERENCES

- [1] Trackman PC. Lysyl oxidase isoforms and potential therapeutic opportunities for fibrosis and cancer [J]. *Expert Opin Ther Targets*, 2016, 20(8): 935-945.
- [2] Li T, Wu C, Gao L, et al. Lysyl oxidase family members in urological tumorigenesis and fibrosis [J]. *Oncotarget*, 2018, 9(28): 20156-20164.
- [3] Wang V, Davis DA, Yarchoan R. Identification of functional hypoxia inducible factor response elements in the human lysyl oxidase gene promoter [J]. *Biochem Biophys Res Commun*, 2017, 490(2): 480-485.
- [4] Kalinichenko VV, Major ML, Wang X, et al. Foxm1b transcription factor is essential for development of hepatocellular carcinomas and is negatively regulated by the p19ARF tumor suppressor [J]. *Genes Dev*, 2004, 18(7): 830-850.
- [5] Chu IM, Michalowski AM, Hoenerhoff M, et al. GATA3 inhibits lysyl oxidase-mediated metastases of human basal triple-negative breast cancer cells [J]. *Oncogene*, 2012, 31(16): 2017-2027.
- [6] Boufraquech M, Nilubol N, Zhang L, et al. miR30a inhibits LOX expression and anaplastic thyroid cancer progression [J]. *Cancer Res*, 2015, 75(2): 367-377.
- [7] Kamikawaji K, Seki N, Watanabe M, et al. Regulation of LOXL2 and SERPINH1 by antitumor microRNA-29a in lung cancer with idiopathic pulmonary fibrosis [J]. *J Hum Genet*, 2016, 61(12): 985-993.
- [8] Kato M, Kurozumi A, Goto Y, et al. Regulation of metastasis-promoting LOXL2 gene expression by antitumor microRNAs in prostate cancer [J]. *J Hum Genet*, 2017, 62(1): 123-132.
- [9] LIU JL, WEI W, TANG W, et al. Mechanism of lysyl oxidase (LOX) in breast cancer invasion and metastasis [J]. *National Medical Journal of China*, 2012, 92(20): 1379-1383. [刘剑仑, 韦薇, 唐玮, 等. 赖氨酰氧化酶在乳腺癌侵袭转移中的作用机制 [J]. *中华医学杂志*, 2012, 92(20): 1379-1383.]
- [10] Zhou ZH, Ji CD, Xiao HL, et al. Reorganized collagen in the tumor microenvironment of gastric cancer and

- its association with prognosis [J] .J Cancer, 2017, 8(8): 1466-1476.
- [11]Baker AM, Cox TR, Bird D,et al.The role of lysyl oxidase in SRC-dependent proliferation and metastasis of colorectal cancer [J] .J Natl Cancer Inst, 2011, 103(5): 407-424.
- [12]Zhan XH, Jiao JW, Zhang HF, et al.A three-gene signature from protein-protein interaction network of LOXL2- and actin-related proteins for esophageal squamous cell carcinoma prognosis [J] .Cancer Med, 2017, 6(7): 1707-1719.
- [13]Le QT, Harris J, Magliocco AM, et al.Validation of lysyl oxidase as a prognostic marker for metastasis and survival in head and neck squamous cell carcinoma: Radiation Therapy Oncology Group trial 90-03 [J] .J Clin Oncol,2009, 27(26): 4281-4286.
- [14]Li RK, Zhao WY, Fang F, et al.Lysyl oxidase-like 4(LOXL4)promotes proliferation and metastasis of gastric cancer via FAK/Src pathway [J] .J Cancer Res Clin Oncol, 2015, 141(2): 269-281.
- [15]Akiri G, Sabo E, Dafni H, et al.Lysyl oxidase-related protein-1 promotes tumor fibrosis and tumor progression in vivo [J] .Cancer Res, 2003, 63(7): 1657-1666.
- [16]Barker HE, Chang J, Cox TR, et al.LOXL2-mediated matrix remodeling in metastasis and mammary gland involution [J] .Cancer Res, 2011, 71(5): 1561-1572.
- [17]Kasashima H, Yashiro M, Kinoshita H, et al.Lysyl oxidase is associated with the epithelial-mesenchymal transition of gastric cancer cells in hypoxia [J] .Gastric Cancer, 2016, 19(2): 431-442.
- [18]Christelle P El-Haibi, George W Bell, Jiangwen Zhang,et al.Critical role for lysyl oxidase in mesenchymal stem cell-driven breast cancer malignancy [J] .Proc Natl Acad Sci USA, 2012,109(43): 17460-17465.
- [19]Yang X, Li S, Li W, et al.Inactivation of lysyl oxidase by  $\beta$ -aminopropionitrile inhibits hypoxia-induced invasion and migration of cervical cancer cells [J] .Oncol Rep, 2013, 29(2): 541-548.
- [20]Peng L, Ran YL, Hu H, et al.Secreted LOXL2 is a novel therapeutic target that promotes gastric cancer metastasis via the Src/FAK pathway [J] .Carcinogenesis, 2009, 30(10): 1660-1669.
- [21]Erler JT, Bennewith KL, Cox TR,et al.Hypoxia-induced lysyl oxidase is a critical mediator of bone marrow cell recruitment to form the premetastatic niche [J] .Cancer Cell, 2009, 15(1): 35-44.
- [22]Wong CC, Zhang H, Gilkes DM, et al.Inhibitors of hypoxia-inducible factor 1 block breast cancer metastatic niche formation and lung metastasis [J] .J Mol Med(Berl), 2012, 90(7): 803-815.
- [23]Kumari S, Panda TK, Pradhan T.Lysyl oxidase: Its diversity in health and diseases [J] .Indian J Clin Biochem, 2017, 32(2): 1-8.
- [24]Reynaud C, Ferreras L, Di MP, et al.Lysyl oxidase is a strong determinant of tumor cell colonization in bone [J] .Cancer Res, 2017, 77(2): 268-278.
- [25]Tang H, Leung L, Saturno G, et al.Lysyl oxidase drives tumour progression by trapping EGF receptors at the cell surface [J] .Nat Commun, 2017 (8) : 14909.
- [26]Ma L, Huang C, Wang XJ, et al.Lysyl oxidase 3 is a dual-specificity enzyme involved in STAT3 deacetylation and deacetylimination modulation [J] .Mol Cell, 2017, 65(2): 296-309.
- [27]Wu G, Guo Z, Chang X, et al.LOXL1 and LOXL4 are epigenetically silenced and can inhibit ras/extracellular signal-regulated kinase signaling pathway in human bladder cancer [J] .Cancer Res, 2007, 67(9): 4123-4129.
- [28]Chang J, Lucas MC, Leonte LE, et al.Pre-clinical evaluation of small molecule LOXL2 inhibitors in breast cancer [J] .Oncotarget, 2017, 8(16): 26066-26078.
- [29]Hecht JR, Rd BA, Vyushkov D, et al.A phase II, randomized, double-blind, placebo-controlled study of simtuzumab in combination with FOLFIRI for the second-line treatment of metastatic KRAS mutant colorectal adenocarcinoma [J] .Oncologist, 2017, 22(3): 243-e23.

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