

赖氨酸琥珀酰化修饰的研究进展

《现代肿瘤医学》[ISSN:1672-4992/CN:61-1415/R] 期数: 2019年20期 页码: 3720-3724 栏目: 综述 出版日期: 2019-09-08

Title: Research progress on lysine succinylation modification

作者: 卢文卿^{1; 2}; 车晓芳^{1; 2}; 郑春雷^{1; 2}; 刘云鹏^{1; 2}

1.中国医科大学附属第一医院肿瘤内科, 辽宁 沈阳 110001; 2.辽宁省肿瘤药物与生物治疗重点实验室, 辽宁 沈阳 110001

Author(s): Lu Wenqing^{1; 2}; Che Xiaofang^{1; 2}; Zheng Chunlei^{1; 2}; Liu Yunpeng^{1; 2}

1.Department of Medical Oncology,the First Hospital of China Medical University,Liaoning Shenyang 110001,China;2.Key Laboratory of Anticancer Drugs and Biotherapy of Liaoning Province,the First Hospital of China Medical University,Liaoning Shenyang 110001,China.

关键词: 琥珀酰化; 琥珀酰基转移酶; 去琥珀酰化酶; 肿瘤

Keywords: succinylation; succinyltransferase; desuccinylase; tumor

分类号: R730

DOI: 10.3969/j.issn.1672-4992.2019.20.040

文献标识码: A

摘要: 琥珀酰化修饰是一种重要的蛋白翻译后修饰 (post-translational modification,PTM) , 可通过调控蛋白酶活性和基因表达, 参与糖代谢、氨基酸代谢、脂肪酸代谢、酮体合成及活性氧清除等多种生命活动。琥珀酰化修饰水平主要受琥珀酰基供体和琥珀酰基转移酶/去琥珀酰化酶的调控, 其异常与包括肿瘤、心脏代谢疾病、肝脏代谢疾病、神经系统疾病等在内的多种疾病的发生发展密切相关。本文拟针对琥珀酰化的基本特点和功能、调控因素及其与疾病的关系作一综述。

Abstract: Succinylation modification is an important post-translational modification (PTM) of proteins.It participates in various life activities such as glucose metabolism,amino acid metabolism,fatty acid metabolism,ketone synthesis and reactive oxygen species scavenging through regulating the activity of substrate protein or gene expression.The level of succinylation modification is mainly regulated by succinyl donors and succinyltransferase/desuccinylase.The aberrant succinylation is closely related to the occurrence and development of various diseases,including tumors,cardiac metabolic diseases,liver metabolic diseases and nervous system diseases.In this article,we aimed to review the basic characteristics and functions of succinylation,its regulatory factors and the relationship between succinylation and diseases.

参考文献/REFERENCES

- [1] Alleyn M,Breitziq M,Lockey R,et al.The dawn of succinylation:A posttranslational modification [J] .Am J Physiol Cell Physiol,2018,314(2):C228-C232.
- [2] Papanicolaou KN,O'rourke B,Foster DB.Metabolism leaves its mark on the powerhouse:Recent progress in post-translational modifications of lysine in mitochondria [J] .Front Physiol,2014(5):301.
- [3] Zhang Z,Tan M,Xie Z,et al.Identification of lysine succinylation as a new post-translational modification [J] .Nat Chem Biol,2011,7(1):58-63.
- [4] Chen H,Xu H,Potash S,et al.Mild metabolic perturbations alter succinylation of mitochondrial proteins [J] .J Neurosci Res,2017,95(11):2244-2252.
- [5] Gibson GE,Xu H,Chen HL,et al.Alpha-ketoglutarate dehydrogenase complex-dependent succinylation of proteins in neurons and neuronal cell lines [J] .J Neurochem,2015,134(1):86-96.
- [6] Smestad J,Erber L,Chen Y,et al.Chromatin succinylation correlates with active gene expression and is perturbed by defective TCA cycle metabolism [J] .Science,2018(2):63-75.
- [7] Zhang Y,Bharathi SS,Rardin MJ,et al.Lysine desuccinylase SIRT5 binds to cardiolipin and regulates the electron transport chain [J] .J Biol Chem,2017,292(24):10239-10249.
- [8] Li L,Shi L,Yang S,et al.SIRT7 is a histone desuccinylase that functionally links to chromatin compaction and genome stability [J] .Nat Commun,2016(7):12235.
- [9] Wang Y,Guo YR,Liu K,et al.KAT2A coupled with the alpha-KGDH complex acts as a histone H3 succinyltransferase [J] .Nature,2017,552(7684):273-277.
- [10] Jing Y,Liu Z,Tian G,et al.Site-specific installation of succinyl lysine analog into histones reveals the effect

- of H2BK34 succinylation on nucleosome dynamics [J]. *Cell Chem Biol*,2018,25(2):166-174.e7.
- [11] Wagner GR,Payne RM.Widespread and enzyme-independent Nepsilon-acetylation and Nepsilon-succinylation of proteins in the chemical conditions of the mitochondrial matrix [J]. *J Biol Chem*,2013,288(40):29036-29045.
- [12] Weinert BT,Scholz C,Wagner SA,et al.Lysine succinylation is a frequently occurring modification in prokaryotes and eukaryotes and extensively overlaps with acetylation [J]. *Cell Rep*,2013,4(4):842-851.
- [13] Bochmann SM,SpieB T,Kotter P,et al.Synthesis and succinylation of subtilin-like lantibiotics are strongly influenced by glucose and transition state regulator AbrB [J]. *Applied and Environmental Microbiology*,2015,81(2):614-622.
- [14] Kurmi K,Hitosugi S,Wiese EK,et al.Carnitine palmitoyltransferase 1A has a lysine succinyltransferase activity [J]. *Cell Rep*,2018,22(6):1365-1373.
- [15] Wang C,Zhang C,Li X,et al.CPT1A-mediated succinylation of S100A10 increases human gastric cancer invasion [J]. *J Cell Mol Med*,2019,23(1):293-305.
- [16] Wang Y,Jin J,Chung MWH,et al.Identification of the YEATS domain of GAS41 as a pH-dependent reader of histone succinylation [J]. *Proc Natl Acad Sci USA*,2018,115(10):2365-2370.
- [17] Du Y,Hu H,Hua C,et al.Tissue distribution,subcellular localization,and enzymatic activity analysis of human SIRT5 isoforms [J]. *Biochem Biophys Res Commun*,2018,503(2):763-769.
- [18] Kumar S,Lombard DB.Functions of the sirtuin deacylase SIRT5 in normal physiology and pathobiology [J]. *Critical Reviews in Biochem Mol Biol*,2018,53(3):311-334.
- [19] Ye XY,Chen ZW,Niu XM,et al.Desuccinylation of pyruvate kinase M2 by SIRT5 contributes to antioxidant response and tumor growth [J]. *Oncotarget*,2017,8(4):6984-6993.
- [20] Kumar S,Lombard DB.Generation and purification of catalytically active recombinant sirtuin5 (SIRT5) protein [J]. *Cancer*,2016(1436):241-257.
- [21] Park J,Chen Y,Tishkoff DX,et al.SIRT5-mediated lysine desuccinylation impacts diverse metabolic pathways [J]. *Mol Cell*,2013,50(6):919-930.
- [22] Yang X,Wang Z,Li X,et al.SHMT2 desuccinylation by SIRT5 drives cancer cell proliferation [J]. *Cancer Res*,2017,78(2):372-386.
- [23] Polletta L,Vernucci E,Carnevale I,et al.SIRT5 regulation of ammonia-induced autophagy and mitophagy [J]. *Autophagy*,2015,11(2):253-270.
- [24] Sadhukhana S,Liu XJ,Ryu D,et al.Metabolomics-assisted proteomics identifies succinylation and SIRT5 as important regulator of cardiac function [J]. *PNAS*,2016,113(16):4320-4325.
- [25] Chen XF,Tian MX,Sun RQ,et al.SIRT5 inhibits peroxisomal ACOX1 to prevent oxidative damage and is downregulated in liver cancer [J]. *EMBO Rep*,2018,19(5):e45124.
- [26] Rardin MJ,He W,Nishida Y,et al.SIRT5 regulates the mitochondrial lysine succinylome and metabolic networks [J]. *Cell Metab*,2013,18(6):920-933.
- [27] Lin ZF,Xu HB,Wang JY,et al.SIRT5 desuccinylates and activates SOD1 to eliminate ROS [J]. *Biochem Biophys Res Commun*,2013,441(1):191-195.
- [28] Zhou L,Wang F,Sun R,et al.SIRT5 promotes IDH2 desuccinylation and G6PD deglutarylation to enhance cellular antioxidant defense [J]. *EMBO Rep*,2016,17(6):811-822.
- [29] Du J,Zhou Y,Su X,et al.Sirt5 is a NAD-dependent protein lysine demalonylase and desuccinylase [J]. *Science*,2011,334(6057):806-809.
- [30] Yokoyama A,Katsura S,Sugawara A.Biochemical analysis of histone succinylation [J]. *Biochem Res Int*,2017(2017):8529404.
- [31] Zhu D,Hou L,Hu B,et al.Crosstalk among proteome,acetylome and succinylome in colon cancer HCT116 cell treated with sodium dichloroacetate [J]. *Sci Rep*,2016(6):37478.
- [32] Li QQ,Hao JJ,Zhang Z,et al.Proteomic analysis of proteome and histone post-translational modifications in heat shock protein 90 inhibition-mediated bladder cancer therapeutics [J]. *Sci Rep*,2017,7(1):201.
- [33] Boylston JA,Sun J,Chen Y,et al.Characterization of the cardiac succinylome and its role in ischemia-reperfusion injury [J]. *J Mol Cell Cardiol*,2015(88):73-81.
- [34] Bai F,Ma Y,Liu Q.Succinylation as a novel mode of energy metabolism regulation during atrial fibrillation [J]. *Medical Hypotheses*,2018(121):54-55.
- [35] Cheng Y,Hou T,Ping J,et al.Quantitative succinylome analysis in the liver of non-alcoholic fatty liver disease rat model [J]. *Proteome Sci*,2016(14):3.
- [36] Liu L,Peritore C,Ginsberg J,et al.Protective role of SIRT5 against motor deficit and dopaminergic degeneration in MPTP-induced mice model of Parkinson's disease [J]. *Behav Brain Res*,2015(281):215-221.
- [37] Lutz M,Milenkovic I,Regelsberger G,et al.Distinct patterns of sirtuin expression during progression of Alzheimer's disease [J]. *Neuromol Med*,2014,16(2):405-414.
- [38] Xie L,Li J,Deng W,et al.Proteomic analysis of lysine succinylation of the human pathogen histoplasma capsulatum [J]. *J Proteomics*,2017(154):109-117.
- [39] Yang Q,Li P,Wen Y,et al.Cadmium inhibits lysine acetylation and succinylation inducing testicular injury of mouse during development [J]. *Toxicol Lett*,2018(291):112-120.

备注/Memo: 国家重点研发计划(编号: 2017YFC1308900); 辽宁省科学技术计划项目(编号: 2015020457); 2015年度留学人员科技活动项目择优资助(项目启动类); 沈阳市重点科技研发计划(编号: 17-230-9-01)

更新日期/Last Update: 1900-01-01