外文医学文献导读： HMGB1、AKT 与心肌缺血再灌注损伤的关系

本次专题检索年限：2022-2024

检索式：(HMGB1 OR AKT) AND (myocardial ischemia reperfusion injury OR MIRI)

使用的数据库：FMRS

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编号：1
题名:Alpha-lipoic acid impedes myocardial ischemia-reperfusion injury, myocardial apoptosis, and oxidative stress by regulating HMGB1 expression.
标题译文:α-硫辛酸通过调节 HMGB1 的表达来阻止心肌缺血再灌注损伤、心肌细胞凋亡和氧化应激。
作 者 :Qi, Bingcai;Zheng, Yue;Gao, Wenqing;Qi, Zhenchang;Gong, Yijie;Liu, Yanwu;Wang, Yuchao;Cheng, Xian;Ning, Meng;Lang, Yuheng;Feng, Jianyu;Li, Tong
出处:EUR J PHARMACOL. 2022-10-15;933:175295.
影响因子:5.0
摘 要 :BACKGROUND:Inflammation, oxidative stress, and apoptosis contribute to myocardial ischemia/reperfusion injury (I/RI). Alpha-lipoic acid (ALA) plays a critical role in I/RI by impeding apoptosis and inflammation. Here, we aimed to explore the underlying mechanisms of ALA after I/RI.METHODS:The left anterior descending coronary artery (LAD) was ligated, and H9c2 cells were exposed to hypoxia/reoxygenation (H/R) to establish an I/RI model. Prior to this, H9c2 cells and rats were treated using an appropriate amount of ALA. The cardiac function, inflammatory factors, and myocardial pathology were assessed in vitro. We detected cell viability, apoptosis, and oxidative stress-related factors in vivo. Moreover, proteins of the HMGB1/TLR4/NF-κB signaling pathway were detected both in vivo and in vitro.RESULTS:We observed that ALA increased cell viability in vitro and decreased apoptosis in vitro and in vivo. ALA inhibited reactive oxygen species production, decreased malondialdehyde, and increased superoxide dismutase activity to resist oxidative stress in vitro. ALA also reduced the expression of inflammatory cytokines (IL-6, IL-1β, and TNF-α) in vivo. ALA also suppressed the levels of the apoptotic protein, Bax, and increased the expression of the anti-apoptotic protein Bcl-2, in vitro and in vivo. Moreover, we observed that ALA significantly inhibited the cytoplasmic localization of HMGB1, which might attenuate MI/RI or H/R via

HMGB1/TLR4/NF-κB pathway.CONCLUSION:ALA regulates HMGB1 translocation and attenuates I/R via the HMGB1/TLR4/NF-κB signaling pathway, thus impeding apoptosis, oxidation, and inflammation, and might be a potential target for myocardial ischemia/reperfusion injury.
主题词:Apoptosis Regulatory Proteins/metabolism;细胞凋亡调控蛋白质/代谢;Cytokines/metabolism;细胞因子类/代谢;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Thioctic Acid*/pharmacology;硫辛酸*/药理学;Thioctic Acid*/therapeutic use;硫辛酸*/治疗应用;Toll-Like Receptor 4/metabolism;类 Toll 受体 4/代谢
全文链接：
https://newfmrs.metstr.com/search/detail?mid=e013c76453217c4b9c8b921c5832c630&searchExp=Alpha-lipoic%20acid%20impedes%20myocardial%20ischemia-reperfusion%20injury,%20myocardial%20apoptosis,%20and%20oxidative%20stress%20by%20regulating%20HMGB1%20expression&

编号：2
题名:Glycyrrhizin attenuates myocardial ischemia reperfusion injury by suppressing Inflammation, oxidative stress, and ferroptosis via the HMGB1-TLR4-GPX4 pathway.
标题译文:甘草甜通过 HMGB1-TLR4-GPX4 途径抑制炎症、氧化应激和铁死亡，从而减轻心肌缺血再灌注损伤。
作者:Zhu, Kaiyi;Fan, Rong;Cao, Yuchen;Yang, Wei;Zhang, Zhe;Zhou, Qiang;Ren, Jie;Shi, Xiushan;Gao, Yuping;Guo, Xiang
出处:EXP CELL RES. 2024-02-01;435(1):113912.
影响因子:3.3
摘要:Ferroptosis, a form of regulated cell death process, play an important role in myocardial ischemia–reperfusion (I/R) injury. Glycyrrhizin (GL), a natural glycoconjugate triterpene, has the property to improve growth rate, immune regulation, antioxidant, anti-inflammatory. However, whether GL can attenuate myocardial I/R injury by modulating ferroptosis or other mechanisms are still unclear. In this study, SD rats underwent in vivo myocardial ischemia/reperfusion (I/R) surgery, while H9C2 cells were subjected to the hypoxia/reoxygenation (H/R) model for in vitro experiments. In addition, TAK-242, a TLR4-specific antagonist, and GL were also used to evaluate the effect and mechanisms of GL on the cardiac function and expression of ferroptosis-related gene and protein in vivo and vitro. The results show that GL decreased not only the expression of the inflammation-related factors (HMGB1, TNF-α, IL-6, IL-18 and IL-1β), but also reduced the number of TUNEL-positive cardiomyocytes, and mitigated pathological alterations in I/R injury. In addition, GL decreased the levels of MDA, promoted antioxidant capacity such as GSH, CAT, Cu/Zn-SOD, Mn-SOD, and SOD in vivo and vitro. More importantly, GL and TAK-242 regulate ferroptosis-related protein and gene expression in I/R and H/R model. Surprisingly, GL may ameliorate cardiomyocyte ferroptosis and ultimately improves cardiac function induced by H/R via the HMGB1-TLR4-GPX4

axis. Therefore, we have highlighted a novel mechanism by which GL regulates inflammation, oxidative stress, and ferroptosis via the HMGB1-TLR4-GPX4 pathway to prevent myocardial I/R injury. GL appears to be a potentially applicable drug for the treatment of myocardial I/R injury.
主题词:Myocardial Reperfusion Injury*/metabolism; 心肌再灌注损伤*/代谢;Glycyrrhizic Acid/pharmacology; 甘草酸/药理学;Toll-Like Receptor 4/metabolism; 类 Toll 受体 4/代谢;Ferroptosis*; 铁死亡*;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Reperfusion Injury*/pathology;再灌注损伤*/病理学;Sulfonamides*;磺胺类*
全文链接：
https://newfmrs.metstr.com/search/detail?mid=e20af0f8fa256070577a2a3b239977f9&searchExp=Glycyrrhizin%20attenuates%20myocardial%20ischemia%20reperfusion%20injury%20by%20suppressing%20Inflammation,%20oxidative%20stress,%20and%20ferroptosis%20via%20the%20HMGB

编号：3
题名:Panaxynol ameliorates cardiac ischemia/reperfusion injury by suppressing NLRP3-induced pyroptosis and apoptosis via HMGB1/TLR4/NF-κB axis.
标题译文:Panaxynol 通过 HMGB1/TLR4/NF-κB 轴抑制 NLRP3 诱导的细胞焦亡和细胞凋亡，从而改善心脏缺血/再灌注损伤。
作者:Ding, Hua-Sheng;Huang, Yan;Qu, Ji-Fu;Wang, Yong-Jian;Huang, Zhong-Yi;Wang, Feng-Yuan;Yi, Wen-Juan;Liu, Xiao-Xiong
出处:INT IMMUNOPHARMACOL. 2023-08-01;121:110222.
影响因子:4.8
摘要:BACKGROUND AND PURPOSE:Panaxynol (PNN) is a common natural minor component in Umbelliferae plants. Many clinical studies have shown that PNN exhibits nutritional value and anti-inflammatory and other pharmacological activities. However, whether PNN can mediate cardiac ischemia/reperfusion injury (IRI) remains unclear. Here, we aimed to determine the potential effects of PNN on myocardial IRI.METHODS:Myocardial IRI was stimulated in a mouse IRI model, and neonatal rat ventricle myocytes (NRVMs) were exposed to hypoxia/reoxygenation to construct in an vitro model. Myocardial infarction size, myocardial tissue injury, myocardial apoptotic index, hemodynamic monitoring, pyroptosis-related proteins, cardiac enzyme activities and inflammatory responses were examined to assess myocardial injury.RESULTS:It was found that PNN administration markedly reduced myocardial infarct size and apoptosis, suppressed myocardial damage and cell pyroptosis, attenuated pro-inflammatory cytokines and neutrophil infiltration via NLRP3 inhibitor. More importantly, PNN treatment remarkably decreased the expression of TLR4/NF-κB pathway-associated proteins and NLRP3-related pyroptosis proteins by HMGB1 inhibitor. PNN also enhanced cell viability, reduced cardiac enzyme activities, suppressed apoptosis and attenuated inflammation in the isolated NRVMs. Furthermore, vitro studies indicated that MCC950 (a NLRP3 inhibitor) increased the anti-inflammatory and anti-apoptotic

effects of PNN on NRVMs via HMGB1/TLR4 pathway.CONCLUSION:To sum up, our results demonstrate that PNN exhibits a cardioprotective effect by modulating heart IRI-induced apoptosis and pyroptosis via HMGB1/TLR4/NF-κB pathway, thereby inhibiting NLRP3 inflammasome stimulation.
主题词:Pyroptosis;细胞焦亡;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Toll-Like Receptor 4/metabolism;类 Toll 受体 4/代谢;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Myocardial Infarction*/metabolism;心肌梗塞*/代谢;
全文链接：
https://newfmrs.metstr.com/search/detail?mid=93a3672ca368b7a4602212198edc560d&searchExp=Panaxynol%20ameliorates%20cardiac%20ischemia%2Freperfusion%20injury%20by%20suppressing%20NLRP3-induced%20pyroptosis%20and%20apoptosis%20via%20HMGB1%2FTLR4%2FNF-%CE%BAB%

编号：4
题名:Enhancing Cardioprotection Through Neutrophil-Mediated Delivery of 18β-Glycyrrhetinic Acid in Myocardial Ischemia/Reperfusion Injury.
标题译文:通过中性粒细胞介导的 18β-甘草次酸输送增强心肌缺血/再灌注损伤中的心脏保护作用。
作者:Han, Dongjian;Wang, Fuhang;Jiang, Qingjiao;Qiao, Zhentao;Zhuang, Yuansong;An, Quanxu;Li, Yuhang;Tang, Yazhe;Li, Chenyao;Shen, Deliang
出处:Adv Sci (Weinh). 2024-09-12;:e2406124.
影响因子:14.3
摘要:Myocardial ischemia/reperfusion injury (MI/RI) generates reactive oxygen species (ROS) and initiates inflammatory responses. Traditional therapies targeting specific cytokines or ROS often prove inadequate. An innovative drug delivery system (DDS) is developed using neutrophil decoys (NDs) that encapsulate 18β-glycyrrhetinic acid (GA) within a hydrolyzable oxalate polymer (HOP) and neutrophil membrane vesicles (NMVs). These NDs are responsive to hydrogen peroxide (H2O2), enabling controlled GA release. Additionally, NDs adsorb inflammatory factors, thereby reducing inflammation. They exhibit enhanced adhesion to inflamed endothelial cells (ECs) and improved penetration. Once internalized by cardiomyocytes through clathrin-mediated endocytosis, NDs protect against ROS-induced damage and inhibit HMGB1 translocation. In vivo studies show that NDs preferentially accumulate in injured myocardium, reducing infarct size, mitigating adverse remodeling, and enhancing cardiac function, all while maintaining favorable biosafety profiles. This neutrophil-based system offers a promising targeted therapy for MI/RI by addressing both inflammation and ROS, holding potential for future clinical applications.
关键词:inflammation; myocardial ischemia - reperfusion injury; nanomedicine; neutrophil decoys (NDs); drug delivery; reactive oxygen species (ROS)
全文链接：

https://newfmrs.metstr.com/search/detail?mid=4b776bafc29bb3f472f84cafcbd02e7d&searchExp=Enhancing%20Cardioprotection%20Through%20Neutrophil-Mediated%20Delivery%20of%2018%CE%B2-Glycyrrhetinic%20Acid%20in%20Myocardial%20Ischemia%2FReperfusion%20Injury&needPu

编号：5
题名:Topical Neck Cooling Without Systemic Hypothermia Attenuates Myocardial Ischemic Injury and Post-ischemic Reperfusion Injury.
标题译文:无需全身低温的局部颈部冷却可减轻心肌缺血损伤和缺血再灌注损伤。
作者:Zhang, Aimee;Rastogi, Radhika;Marsh, Katherine M;Yang, Boris;Wu, Di;Kron, Irving L;Yang, Zequan
出处:Front Cardiovasc Med. 2022-01-01;9:893837.
影响因子:3.6
摘 要 :BACKGROUND:Following acute myocardial infarction (MI), irreversible damage to the myocardium can only be reduced by shortening the duration between symptom onset and revascularization. While systemic hypothermia has shown promising results in slowing pre-revascularization myocardial damage, it is resource intensive and not conducive to prehospital initiation. We hypothesized that topical neck cooling (NC), an easily implemented therapy for en route transfer to definitive therapy, could similarly attenuate myocardial ischemia-reperfusion injury (IRI).METHODS:Using an in vivo mouse model of myocardial IRI, moderate systemic hypothermia or NC was applied following left coronary artery (LCA) occlusion and subsequent reperfusion, at early, late, and post-reperfusion intervals. Vagotomy was performed after late NC in an additional group. Hearts were harvested to measure infarct size.RESULTS:Both hypothermia treatments equally attenuated myocardial infarct size by 60% compared to control. The infarct-sparing effect of NC was temperature-dependent and timing-dependent. Vagotomy at the gastroesophageal junction abolished the infarct-sparing effect of late NC. Cardiac perfusate isolated following ischemia had significantly reduced cardiac troponin T, HMGB1, cell-free DNA, and interferon α and β levels after NC.CONCLUSIONS:Topical neck cooling attenuates myocardial IRI in a vagus nerve-dependent manner, with an effect comparable to that of systemic hypothermia. NC attenuated infarct size when applied during ischemia, with earlier initiation resulting in superior infarct sparing. This novel therapy exerts a cardioprotective effect without requiring significant change in core temperature and may be a promising practical strategy to attenuate myocardial damage while patients await definitive revascularization.
关 键 词 :therapeutic hypothermia, myocardial infarction, topical hypothermia, ischemia-reperfusion injury, vagal activation
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9274088/

编号：6
题名:Amelioration of myocardial ischemia/reperfusion injury in diabetes: A narrative review of the mechanisms and clinical applications of dexmedetomidine.
标题译文:改善糖尿病心肌缺血/再灌注损伤：右美托咪定机制和临床应用的叙述性综述。
作者:Sun, Meng;Wang, Rong;Xia, Rui;Xia, Zhengyuan;Wu, Zhilin;Wang, Tingting
出处:Front Pharmacol. 2022-01-01;13:949754.
影响因子:5.6
摘 要 :Mechanisms contributing to the pathogenesis of myocardial ischemia-reperfusion (I/R) injury are complex and multifactorial. Many strategies have been developed to ameliorate myocardial I/R injuries based on these mechanisms. However, the cardioprotective effects of these strategies appear to diminish in diabetic states. Diabetes weakens myocardial responses to therapies by disrupting intracellular signaling pathways which may be responsible for enhancing cellular resistance to damage. Intriguingly, it was found that Dexmedetomidine (DEX), a potent and selective α2-adrenergic agonist, appears to have the property to reverse diabetes-related inhibition of most intervention-mediated myocardial protection and exert a protective effect. Several mechanisms were revealed to be involved in DEX's protection in diabetic rodent myocardial I/R models, including PI3K/Akt and associated GSK-3β pathway stimulation, endoplasmic reticulum stress (ERS) alleviation, and apoptosis inhibition. In addition, DEX could attenuate diabetic myocardial I/R injury by up-regulating autophagy, reducing ROS production, and inhibiting the inflammatory response through HMGB1 pathways. The regulation of autonomic nervous function also appeared to be involved in the protective mechanisms of DEX. In the present review, the evidence and underlying mechanisms of DEX in ameliorating myocardial I/R injury in diabetes are summarized, and the potential of DEX for the treatment/prevention of myocardial I/R injury in diabetic patients is discussed.
关 键 词 :cardioprotection, ischemia-reperfusion, oxidative stress, autophagy, inflammation, apoptosis, dexmedetomidine
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9470922/

编号：7
题 名 :Recombinant Klotho Protein Ameliorates Myocardial Ischemia/Reperfusion Injury by Attenuating Sterile Inflammation.
标题译文:重组 Klotho 蛋白通过减弱无菌炎症来改善心肌缺血/再灌注损伤。
作 者 :Myung, Jinwoo;Beom, Jin-Ho;Kim, Ju-Hee;Woo, Ji-Sun;Park, Incheol;Chung, Sung-Phil;Chung, Yong-Eun;You, Je-Sung
出处:Biomedicines. 2022-04-13;10(4)
影响因子:4.7
摘 要 :Currently, no effective therapy and potential target have been elucidated for preventing myocardial ischemia and reperfusion injury (I/R). We hypothesized that the administration of recombinant klotho (rKL) protein could attenuate the sterile

inflammation in peri-infarct regions by inhibiting the extracellular release of high mobility group box-1 (HMGB1). This hypothesis was examined using a rat coronary artery ligation model. Rats were divided into sham, sham+ rKL, I/R, and I/R+ rKL groups (n = 5/group). Administration of rKL protein reduced infarct volume and attenuated extracellular release of HMGB1 from peri-infarct tissue after myocardial I/R injury. The administration of rKL protein inhibited the expression of pro-inflammatory cytokines in the peri-infarct regions and significantly attenuated apoptosis and production of intracellular reactive oxygen species by myocardial I/R injury. Klotho treatment significantly reduced the increase in the levels of circulating HMGB1 in blood at 4 h after myocardial ischemia. rKL regulated the levels of inflammation-related proteins. This is the first study to suggest that exogenous administration of rKL exerts myocardial protection effects after I/R injury and provides new mechanistic insights into rKL that can provide the theoretical basis for clinical application of new adjunctive modality for critical care of acute myocardial infarction.

关键词: acute myocardial infarction, klotho, myocardial ischemia/reperfusion injury, high mobility group box-1, sterile inflammation

全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9032004/

编号：8

题名:Berberine up-regulates miR-340-5p to protect myocardial ischaemia/reperfusion from HMGB1-mediated inflammatory injury.

标题译文:Berberine 上调 miR-340-5p 以保护心肌缺血/再灌注免受 HMGB1 介导的炎症损伤。

作 者 :Long, Tianyi;Pan, Wei;Li, Fei;Sheikh, Sayed Ali;Xie, Qiying;Zhang, Chenglong

出处:ESC Heart Fail. 2023-04-01;10(2):931-942.

影响因子:3.2

摘要:AIMS:Myocardial ischaemia/reperfusion injury (MIRI) is a major cause of heart failure after myocardial infarction. Berberine (BBR) presents anti-inflammatory and immunosuppressive properties in many diseases. Our research looked into the therapeutic effects and mechanism of BBR in MIRI.METHODS AND RESULTS:MIRI animal and cell models were established. The mRNA and protein expressions were assessed using reverse transcription and quantitative real-time polymerase chain reaction and western blot. The haemodynamic parameters (left ventricular ejection fraction and left ventricular ejection fraction) were detected by echocardiography. The myocardial infarct size and myocardium lesion were assessed by triphenyltetrazolium chloride and haematoxylin-eosin staining. The levels of injury factors were determined by ELISA. Terminal deoxynucleotidyl transferase-mediated dUTP nick-end labelling staining was performed to analyse cell apoptosis. Dual luciferase reporter gene and RNA immunoprecipitation assays were carried out to verify the interaction between miR-340-5p and HMGB1. BBR administration could improve the haemodynamic parameters and infarct size in MIRI rats (all $P < 0.05$). In

MIRI rat model, BBR reduced cardiomyocyte apoptosis and inflammation (all $P < 0.05$). BBR could promote miR-340-5p expression (0.64 ± 0.21, $P < 0.05$), which is lowly expressed in MIRI group (0.24 ± 0.10, $P < 0.01$) in compare with the sham group (0.99 ± 0.01). MiR-340-5p knockdown abolished the protective effects of BBR on H/R-treated cardiomyocytes (all $P < 0.05$). BBR suppressed the HMGB1/TLR4/NF-κB pathway activation in MIRI. HMGB1 functioned as the target of miR-340-5p, and its silencing reversed the effect of miR-340-5p inhibitor on BBR-treated MIRI.CONCLUSIONS:In MIRI, BBR repressed HMGB1-mediated TLR4/NF-κB signalling pathway through miR-340-5p to suppress cardiomyocyte apoptosis and inflammation.
主题词:Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Berberine*/pharmacology;小檗碱*/药理学;Berberine*/therapeutic use;小檗碱*/治疗应用;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;MicroRNAs*/genetics;微RNAs*/遗传学;MicroRNAs*/metabolism;微RNAs*/代谢;Myocardial Ischemia*/drug therapy;心肌缺血*/药物疗法;Myocardial Infarction*/genetics;心肌梗塞*/遗传学;Coronary Artery Disease*;冠状动脉病变*;
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10053273/

编号：9
题名:Short-term pretreatment of naringin isolated from Citrus wilsonii Tanaka attenuates rat myocardial ischemia/reperfusion injury.
标题译文:从 Citrus wilsonii Tanaka 中分离出的柚皮苷的短期预处理可减轻大鼠心肌缺血/再灌注损伤。
作者:Liu, Wenting;Cheng, Liping;Li, Xuefei;Zhao, Lili;Hu, Xiaorong;Ma, Zhaocheng
出处:N-S ARCH PHARMACOL. 2022-09-01;395(9):1047-1059.
影响因子:3.6
摘要:Pretreatment or treatment with anti-apoptotic, anti-inflammatory, or anti-oxidative approaches could be critical for attenuated the severity of myocardial ischemia/reperfusion (I/R) injury. Naringin, a natural flavonoid, plays important roles in inflammation-related diseases. Immature dry fruits of Citrus wilsonii Tanaka (Xiang Yuan) are rich in naringin that can be used as traditional Chinese medicine to treat inflammation-related symptoms. However, its roles in cardioprotective role remain unclear. This study aimed to isolate naringin from Citrus wilsonii Tanaka fruit and tested their cardioprotective effect. The dry fruits of Citrus wilsonii Tanaka were extracted with boiling water and then supernatants were freeze-dried to yield aqueous extract (ZQAE). The extract was chemoprofiled using UPLC-MS/MS to stand for major constituents, and then subjected to different chromatographic separation steps, and naringin was isolated in a high yield. The cardioprotective effects of the aqueous extract of ZQAE and naringin were investigated in a myocardial I/R rat model and to elucidate the mechanism underlying its cardioprotective effect. Our results indicated that 5-day ZQAE and naringin pretreatments both promoted histopathological changes and reduced myocardial enzymes (cTnl, CK-MB, CK and LDH) induced by

I/R. Moreover, the 50 mg/kg and 100 mg/kg ZQAE dose pretreatments presented a significantly decreased infarct size as well as myocardial enzyme levels but also inhibited myocardial apoptosis (cleaved-caspase3 protein expression), the inflammatory response (IL-23, IL-6, and TNF-α) and oxidative stress (MDA and SOD). The cardioprotective effect of 5 mg/kg dose of naringin pretreatment is comparable with that of 5 mg/kg drug ditiazem pretreatment. Additionally, naringin pretreatment exhibited striking decreases in the apoptosis index and downregulation of the protein expression levels of cleaved-Caspase3, Bcl2 and Bax. Meanwhile, naringin downregulated HMGB1 expression and upregulated SIRT1 expression in the myocardium. These findings suggest that short-term pretreatments with ZQAE and naringin both protect against myocardial I/R injury by suppressing myocardial apoptosis, the inflammatory response, and oxidative stress. The cardioprotective effect of naringin involves SIRT1 activation and may interact with HMGB1 and inhibit the release of HMGB1.
主题词:Apoptosis;细胞凋亡;Citrus*;柑桔属*;Flavanones;黄烷酮类;HMGB1 Protein*;HMGB1 蛋白*;Myocardial Reperfusion Injury*;心肌再灌注损伤*
全文链接：
https://newfmrs.metstr.com/search/detail?mid=583c6bff109e6877fa7dc6f31ba26b73&searchExp=Short-term%20pretreatment%20of%20naringin%20isolated%20from%20Citrus%20wilsonii%20Tanaka%20attenuates%20rat%20myocardial%20ischemia%2Freperfusion%20injury&needPubmedPar

编号：10
题名:High mobility group box 1 derived mainly from platelet microparticles exacerbates microvascular obstruction in no reflow.
标题译文:主要来自血小板微粒的高迁移率组框 1 加剧了无回流的微血管阻塞。
作者:Zhao, Xinyi;Han, Jianbin;Zhou, Lijin;Zhao, Jinjin;Huang, Meijiao;Wang, Yueqing;Kou, Junjie;Kou, Yan;Jin, Jiaqi
出处:THROMB RES. 2023-02-01;222:49-62.
影响因子:3.7
摘要:INTRODUCTION:No reflow manifests coronary microvascular injury caused by continuous severe myocardial ischemia and reperfusion. Microvascular obstruction (MVO) has emerged as one fundamental mechanism of no reflow. However, the underlying pathophysiology remains incompletely defined. Herein, we explore the contribution of high mobility group box 1 (HMGB1), derived mainly from platelet microparticles exacerbating MVO in no reflow.MATERIALS AND METHODS:44 STEMI patients undergoing successful primary percutaneous coronary intervention (PCI) were included in our study. Plasma HMGB1 levels in both the peripheral artery (PA) and infarct-related coronary artery (IRA) were measured by ELISA. Flow cytometry and confocal microscopy assessed the level of HMGB1+ platelet derived microparticles (PMPs) and platelet activation. Flow cytometry and western blot evaluated the procoagulant activity (PCA) and the release of inflammatory factors of

human microvascular endothelial cells (HCEMCs).RESULTS:HMGB1 levels were significantly higher in the IRA in no-reflow patients. The levels of HMGB1+ PMPs were considerably higher in the IRA of patients with no reflow and were strongly associated with platelet activation. Moreover, our results show that HMGB1 interacts with human microvascular endothelial cells primarily through TLR4, inducing HCMEC proinflammatory, procoagulant phenotype, and monocyte recruitment, accelerating microvascular obstruction and facilitating the development of no reflow.CONCLUSION:Our results illustrate a novel mechanism by which HMGB1, derived mainly from PMPs, plays a crucial role in the pathogenesis of no-reflow, revealing a novel therapeutic target.
主题词:Myocardial Infarction*;心肌梗塞*;Percutaneous Coronary Intervention*;经皮冠状动脉介入治疗*;Cell-Derived Microparticles*;细胞衍生微粒*;HMGB1 Protein*;HMGB1 蛋白*;Coronary Circulation;冠状动脉循环;
全文链接：
https://newfmrs.metstr.com/search/detail?mid=401f9be90a072bdbec22f95207ce705e&searchExp=High%20mobility%20group%20box%201%20derived%20mainly%20from%20platelet%20microparticles%20exacerbates%20microvascular%20obstruction%20in%20no%20reflow&needPubmedParse=f

编号：11
题名:Aucubin protects against myocardial ischemia-reperfusion injury by regulating STAT3/NF-κB/HMGB-1 pathway.
标题译文:Aucubin 通过调节 STAT3/NF-κB/HMGB-1 通路来保护心肌缺血再灌注损伤。
作者:Liu, Yanwu;Cheng, Xian;Qi, Bingcai;Wang, Yuchao;Zheng, Yue;Liang, Xiaoyu;Chang, Yun;Ning, Meng;Gao, Wenqing;Li, Tong
出处:INT J CARDIOL. 2024-04-01;400:131800.
影响因子:3.2
摘要:The main characteristics of the myocardial ischemia/reperfusion injury (MI/RI) are oxidative stress, apoptosis, and an inflammatory response. Aucubin (AU) is an iridoid glycoside that possesses various biological properties and has been discovered to demonstrate antioxidant and anti-inflammatory impacts in pathological processes, such as ischemia-reperfusion. The objective of this research was to investigate if AU treatment could mitigate myocardial inflammation and apoptosis caused by ischemia/reperfusion (I/R) in both laboratory and animal models, and to elucidate its underlying mechanism. By ligating the coronary artery on the left anterior descending side, a successful MI/RI rat model was created. Additionally, H9C2 cells were subjected to hypoxia/reoxygenation (H/R) in order to imitate the injury caused by ischemia/reperfusion (I/R). Furthermore, various concentrations of AU were administered to H9C2 cells or rats before H/R stimulation or myocardial I/R surgery, respectively. In vitro, the assessment was conducted on cardiac function, inflammatory markers, and myocardial pathology. In vivo, we examined the viability of cells, as well as factors related to apoptosis and oxidative stress. Furthermore, the

presence of proteins belonging to the STAT3/NF-κB/HMGB1 signaling pathway was observed both in vivo and in vitro. AU effectively improved cardiomyocyte injury caused by H/R and myocardial injury caused by I/R. Furthermore, AU suppressed the production of reactive oxygen species and inflammatory molecules (TNF-alpha, IL-1β, and IL-6) and proteins associated with cell death (caspase-3 and Bax), while enhancing the levels of anti-inflammatory agents (IL-10) and the anti-apoptotic protein Bcl-2.AU mechanistically affected the phosphorylation of STAT3 at the Ser727 site and Tyr705 following H/R by modulating the signaling pathway involving signal transducer and activator of transcription 3 (STAT3)/nuclear factor-κB (NF-κB)/high mobility group box 1 (HMGB1), while also suppressing the nuclear translocation of NF-κB p65 and HMGB1 exonucleation. In conclusion, the use of AU treatment might offer protection against myocardial infarction and injury by reducing oxidative stress, suppressing apoptosis, and mitigating inflammation. The regulation of the STAT3/NF-κB/HMGB-1 pathway may contribute to this phenomenon by affecting STAT3 phosphorylation and controlling NF-κB and HMGB-1 translocation. Contributes to identifying possible objectives for myocardial ischemia/reperfusion damage.

主题词:Myocardial Reperfusion Injury*/metabolism; 心肌再灌注损伤*/代谢;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Apoptosis; 细胞凋亡;Myocardial Infarction*; 心肌梗塞*;Reperfusion Injury*; 再灌注损伤*;Iridoid Glucosides*;环烯醚萜葡糖苷类*

全文链接：

https://newfmrs.metstr.com/search/detail?mid=b68c9de15597cc619b4b68c6047cdbc9&searchExp=%28Aucubin%20protects%20against%20myocardial%20ischemia-reperfusion%20injury%20by%20regulating%20STAT3%2FNF-%CE%BAB%2FHMGB-1%20pathway%29%20AND%202022%3A2025%5Bdp%5D&ne

编号：12

题名:High Mobility Group Box 1 and Cardiovascular Diseases: Study of Act and Connect.

标题译文:高迁移率族蛋白 B1 与心血管疾病：Act and Connect 研究。

作者:Wasim, Rufaida;Singh, Aditya;Islam, Anas;Mohammed, Saad;Anwar, Aamir;Mahmood, Tarique

出处:CARDIOVASC TOXICOL. 2024-11-01;24(11):1268-1286.

影响因子:3.4

摘要:Cardiovascular disease is the deadly disease that can result in sudden death, and inflammation plays an important role in its onset and progression. High mobility group box 1 (HMGB1) is a nuclear protein that regulates transcription, DNA replication, repair, and nucleosome assembly. HMGB1 is released passively by necrotic tissues and actively secreted by stressed cells. Extracellular HMGB1 functions as a damage associated molecular patterns molecule, producing numerous redox forms that induce a range of cellular responses by binding to distinct receptors

and interactors, including tissue inflammation and regeneration. Extracellular HMGB1 inhibition reduces inflammation and is protective in experimental models of myocardial ischemia/reperfusion damage, myocarditis, cardiomyopathies caused by mechanical stress, diabetes, bacterial infection, or chemotherapeutic drugs. HMGB1 administration following a myocardial infarction followed by permanent coronary artery ligation improves cardiac function by stimulating tissue regeneration. HMGB1 inhibits contractility and produces hypertrophy and death in cardiomyocytes, while also stimulating cardiac fibroblast activity and promoting cardiac stem cell proliferation and differentiation. Maintaining normal nuclear HMGB1 levels, interestingly, protects cardiomyocytes from apoptosis by limiting DNA oxidative stress, and mice with HMGB1cardiomyocyte-specific overexpression are partially protected from cardiac injury. Finally, elevated levels of circulating HMGB1 have been linked to human heart disease. As a result, following cardiac damage, HMGB1 elicits both detrimental and helpful responses, which may be due to the formation and stability of the various redox forms, the particular activities of which in this context are mostly unknown. This review covers recent findings in HMGB1 biology and cardiac dysfunction.

主题词:HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Cardiovascular Diseases*/metabolism;心血管疾病*/代谢;Cardiovascular Diseases*/physiopathology;心血管疾病*/病理生理学;Cardiovascular Diseases*/pathology;心血管疾病*/病理学;Cardiovascular Diseases*/prevention & control;心血管疾病*/预防与控制;Signal Transduction*;信号传导*;

全文链接：

https://newfmrs.metstr.com/search/detail?mid=576199a4478943a15c030292e47ff738&searchExp=High%20Mobility%20Group%20Box%201%20and%20Cardiovascular%20Diseases%3A%20Study%20of%20Act%20and%20Connect&needPubmedParse=false&query=High%20Mobility%20Group%20Box%201%

编号：13

题名:HMGB1-RAGE axis contributes to myocardial ischemia/reperfusion injury via regulation of cardiomyocyte autophagy and apoptosis in diabetic mice.

标题译文:HMGB1-RAGE 轴通过调节糖尿病小鼠心肌细胞自噬和凋亡而导致心肌缺血/再灌注损伤。

作者:He, De-Wei;Liu, De-Zhao;Luo, Xiao-Zhi;Chen, Chuan-Bin;Lu, Chuang-Hong;Na, Na;Huang, Feng

出处:BIOL CHEM. 2024-03-25;405(3):167-176.

影响因子:2.9

摘要:Patients with acute myocardial infarction complicated with diabetes are more likely to develop myocardial ischemia/reperfusion (I/R) injury (MI/RI) during reperfusion therapy. Both HMGB1 and RAGE play important roles in MI/RI. However, the specific mechanisms of HMGB1 associated with RAGE are not fully clarified in diabetic MI/RI. This study aimed to investigate whether the HMGB1-RAGE axis induces diabetic MI/RI via regulating autophagy and apoptosis. A db/db

mouse model of MI/RI was established, where anti-HMGB1 antibody and RAGE inhibitor (FPS-ZM1) were respectively injected after 10 min of reperfusion. The results showed that treatment with anti-HMGB1 significantly reduced the infarct size, serum LDH, and CK-MB level. Similar situations also occurred in mice administrated with FPS-ZM1, though the HMGB1 level was unchanged. Then, we found that treatment with anti-HMGB1 or FPS-ZM1 performed the same effects in suppressing the autophagy and apoptosis, as reflected by the results of lower LAMP2 and LC3B levels, increased Bcl-2 level, reduced BAX and caspase-3 levels. Moreover, the Pink1/Parkin levels were also inhibited at the same time. Collectively, this study indicates that the HMGB1-RAGE axis aggravated diabetic MI/RI via apoptosis and Pink1/Parkin mediated autophagy pathways, and inhibition of HMGB1 or RAGE contributes to alleviating those adverse situations.
主题词:Apoptosis;细胞凋亡;Benzamides*;苯甲酰胺类*;Diabetes Mellitus, Experimental*/complications;糖尿病,实验性*/并发症;Diabetes Mellitus, Experimental*/metabolism;糖尿病,实验性*/代谢;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;
全文链接：
https://newfmrs.metstr.com/search/detail?mid=e713ea67c4b32bd8024a783ea9ca45a4&searchExp=HMGB1-RAGE%20axis%20contributes%20to%20myocardial%20ischemia%2Freperfusion%20injury%20via%20regulation%20of%20cardiomyocyte%20autophagy%20and%20apoptosis%20in%20diabeti

编号：14
题名:Lipopolysaccharides protect mesenchymal stem cell against cardiac ischemia-reperfusion injury by HMGB1/STAT3 signaling.
标题译文:脂多糖通过 HMGB1/STAT3 信号传导保护间充质干细胞免受心脏缺血再灌注损伤。
作者:Wen, Jing-Yi;Peng, Hui-Xi;Wang, Dan;Wen, Zhi-Min;Liu, Yu-Tong;Qu, Jian;Cui, Hong-Xuan;Wang, Yu-Ying;DU, Yan-Lin;Wang, Ting;Geng, Cong;Xu, Bing
出处:J GERIATR CARDIOL. 2023-11-28;20(11):801-812.
影响因子:1.8
摘要:BACKGROUND:Myocardial ischemia-reperfusion (I/R) is a serious and irreversible injury. Bone marrow-derived mesenchymal stem cells (MSCs) is considered to be a potential therapy for I/R injury due to the paracrine effects. High-mobility group box 1 (HMGB1) is a novel mediator in MSC and regulates the response of inflammation injury. Signal Transduction and Transcription Activator 3 (STAT3) is a critical transcription factor and important for release of paracrine factors. However, the relationship between HMGB1 and STAT3 in paracrine effect of MSC remains unknown.METHODS:In vitro, hypoxia/reoxygenation injury model was established by AnaeroPack System and examined by Annexin V flow cytometry,

CCK8 assay and morphology observation. Detection of apoptotic proteins and protein expression of HMGB1 and STAT3 by Western blot.RESULTS:The conditioned medium of MSCs with or without LPS pretreatment was cocultured with H9C2 cells for 24 h before hypoxia treatment and MSC showed obvious cardiomyocytes protect role, as evidence by decreased apoptosis rate and improved cells viability, and LPS pretreated MSC exhibited better protect role than untreated MSC. However, such effect was abolished in HMGB1 deficiency group, silencing HMGB1 decreased the secretion of vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), insulin growth factor (IGF), cell viability, and the expression of STAT3. Furthermore, STAT3 silence attenuated the protective effect of LPS in MSC.CONCLUSIONS:These findings suggested that LPS improved MSC-mediated cardiomyocytes protection by HMGB1/STAT3 signaling.
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10716610/

编号：15
题名:Influences of microRNA-451 on the expression of HMGB1 in myocardial cells and its mechanism in ischemia-reperfusion injury.
标题译文:microRNA-451 对心肌细胞 HMGB1 表达的影响及其在缺血再灌注损伤中的机制
作者:Qiu, Ruiye;Zhang, Yajuan;Li, Jun;Wu, Jun;He, Ruifeng
出处:CELL MOL BIOL. 2023-12-31;69(15):141-147.
影响因子:1.5
摘要:This work aimed to understand the underlying mechanism of micro-ribonucleic acid (MicroRNA) (miR)-451 in ischemia-reperfusion injury (IRI) and the influences of miR-451 on high mobility group box 1 protein (HMGB1) in myocardial cells, 30 specific pathogen-free (SPF) male rats were selected and randomly rolled into 5 groups, which were a sham operation control (Control), an ischemia-reperfusion (I/R), aI/R+Ad-GFP, amiR-451 up-regulation (I/R+Ad-miR-451), and a miR-451 down-regulation groups (I/R+Ad-asmiR-451). There were 6 cases in each group. Myocardial cell apoptosis, the contents of serum lactic acid dehydrogenase (LDH), creatine kinase (CK), and malondialdehyde (MDA), the activity of superoxide dismutase (SOD), and the expressions of miR-451 and HMGB1mRNA were detected. Relative to those in I/R and I/R+Ad-GFP groups, the expressions of CD3+, CD4+, and CD4+/ CD8+ in I/R+Ad-miR-451 group reduced (P<0.05). The expressions of serum LDH and CK decreased (P<0.05). In contrast, MDA content and SOD activity enhanced (P<0.05). HMGB1 and Cleaved-caspase3 declined (P<0.05). Besides, miR-451 improved while the expression of HMGB1mRNA significantly reduced (P<0.05). miR-451 can regulate the expressions of HMGB1mRNA and its protein at the transcriptional level. miR-451 up-regulation can inhibit HMGB1 expression, relieve IRI, and protect myocardial cells, which may be achieved by improving oxidative stress injury and inhibiting cell apoptosis.
主题词:HMGB1 Protein*/genetics;HMGB1 蛋白*/遗传学;HMGB1 Protein*/metabolism;HMGB1 蛋白*/代谢;MicroRNAs*/genetics;微 RNAs*/遗传

学 ;MicroRNAs*/metabolism; 微 RNAs*/ 代 谢 ;Myocardial Reperfusion Injury*/genetics; 心 肌 再 灌 注 损 伤 */ 遗 传 学 ;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;
全文链接：
https://newfmrs.metstr.com/search/detail?mid=e5248c71b29eac2fe5f8851fd54df244&searchExp=Influences%20of%20microRNA-451%20on%20the%20expression%20of%20HMGB1%20in%20myocardial%20cells%20and%20its%20mechanism%20in%20ischemia-reperfusion%20injury&needPubmedPar

编号：16
题名:Panax notoginseng saponins dually modulates autophagy in gastric precancerous lesions complicated with myocardial ischemia-reperfusion injury model through the PI3K/AKT/mTOR pathway.
标题译文:三七总皂苷通过 PI3K/AKT/mTOR 通路双重调节胃癌前病变合并心肌缺血再灌注损伤模型中的自噬。
作者:Wang, Xiaoyan;Zhang, Ruihang;Zeng, Nili;Li, Hao;Hua, Baojin
出处:BIOMED PHARMACOTHER. 2024-09-01;178:117268.
影响因子:6.9
摘 要 :Gastric precancerous lesion (GPL) is a crucial stage in the development of gastric cancer, characterized by incomplete intestinal epithelial chemotaxis and heterogeneous hyperplasia with high malignant potential. Early intervention in GPL is vital for preventing gastric cancer. Additionally, there are shared risk factors and pathogenesis between tumors and coronary heart disease (CHD), with an increasing number of tumor patients GPL complicated with CHD due to improved survival rates. Reperfusion therapy in CHD can result in myocardial ischemia-reperfusion injury (MIRI). Traditional Chinese medicine (TCM) has demonstrated unique advantages in treating GPL and MIRI by promoting blood circulation and removing blood stasis. Panax ginseng total saponin (PNS), a component of TCM known for its blood circulation benefits, has shown positive effects in inhibiting tumor growth and improving myocardial ischemia. This study utilized a GPL-MIRI mouse model to investigate the effects of PNS in treatment. Results indicated that PNS significantly improved typical GPL lesions in mice, such as incomplete intestinal epithelialization and heteroplasia, and also reduced myocardial infarction. At the molecular level, PNS exhibited a bidirectional regulatory role in the GPL-MIRI model. It enhanced the autophagic process in gastric mucosal cells by inhibiting the PI3K/Akt/mTOR signaling pathway, while suppressed excessive autophagy in cardiomyocytes. These findings offer new insights and treatment strategies for managing GPL and MIRI using the TCM compound PNS.
主 题 词 :Autophagy*/drug effects; 自 吞 噬 */ 药 物 作 用 ;Myocardial Reperfusion Injury*/drug therapy; 心 肌 再 灌 注 损 伤 */ 药 物 疗 法 ;Myocardial Reperfusion Injury*/pathology; 心 肌 再 灌 注 损 伤 */ 病 理 学 ;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Panax notoginseng*/chemistry;三七*/化

学 ;Proto-Oncogene Proteins c-akt/metabolism; 原 癌 基 因 蛋 白 质 c-akt/ 代谢;Saponins*/pharmacology;皂苷类*/药理学;Saponins*/therapeutic use;皂苷类*/治疗 应 用 ;Signal Transduction*/drug effects; 信 号 传 导 */ 药 物 作 用 ;Stomach Neoplasms*/drug therapy;胃肿瘤*/药物疗法;Stomach Neoplasms*/pathology;胃肿瘤*/病理学;Stomach Neoplasms*/metabolism;胃肿瘤*/代谢
全文链接：
https://newfmrs.metstr.com/search/detail?mid=5b2c0d1e709fd476cfa54ecaae52647e&searchExp=Panax%20notoginseng%20saponins%20dually%20modulates%20autophagy%20in%20gastric%20precancerous%20lesions%20complicated%20with%20myocardial%20ischemia-reperfusion%20injur

编号：17
题名:Knockdown of forkhead box protein P1 alleviates hypoxia reoxygenation injury in H9c2 cells through regulating Pik3ip1/Akt/eNOS and ROS/mPTP pathway.
标题译文:叉头盒蛋白 P1 的敲低通过调节 Pik3ip1/Akt/eNOS 和 ROS/mPTP 通路减轻 H9c2 细胞缺氧复氧损伤。
作 者 :Liu, Xinming;Yang, Yixing;Song, Jiawei;Li, Dongjie;Liu, Xiaoyan;Li, Chuang;Ma, Zheng;Zhong, Jiuchang;Wang, Lefeng
出处:BIOENGINEERED. 2022-01-01;13(1):1320-1334.
影响因子:4.9
摘要:Forkhead box protein P1 (Foxp1) exerts an extensive array of physiological and pathophysiological impacts on the cardiovascular system. However, the exact function of myocardial Foxp1 in myocardial ischemic reperfusion injury (MIRI) stays largely vague. The hypoxia reoxygenation model of H9c2 cells (the rat ventricular myoblasts) closely mimics myocardial ischemia-reperfusion injury. This report intends to research the effects and mechanisms underlying Foxp1 on H9c2 cells in response to hypoxia (12 h)/reoxygenation (4 h) (HR) stimulation. Expressions of Foxp1 and Phosphatidylinositol 3-kinase interacting protein 1 (Pik3ip1) were both upregulated in ischemia/reperfusion (IR)/HR-induced injury. Stimulation through HR led to marked increases in cellular apoptosis, mitochondrial dysfunction, and superoxide generation in H9c2 cells, which were rescued with knockdown of Foxp1 by siRNA. Silence of Foxp1 depressed expression of Pik3ip1 directly activated the PI3K/Akt/eNOS pathway and promoted nitric oxide (NO) release. Moreover, the knockdown of Foxp1 blunted HR-induced enhancement of reactive oxygen species (ROS) generation, thus alleviating excessive persistence of mitochondrial permeability transition pore (mPTP) opening and decreased mitochondrial apoptosis-associated protein expressions in H9c2 cells. Meanwhile, these cardioprotective effects can be abolished by LY294002, NG-nitro-L-arginine methyl ester (L-NAME), and Atractyloside (ATR), respectively. In summary, our findings indicated that knockdown of Foxp1 prevented HR-induced encouragement of apoptosis and oxidative stress via PI3K/Akt/eNOS signaling activation by targeting Pik3ip1 and improved mitochondrial function by inhibiting ROS-mediated mPTP opening. Inhibition of Foxp1 may be a promising therapeutic avenue for MIRI.

主题词:Forkhead Transcription Factors/genetics*;叉头转录因子/遗传学*;Forkhead Transcription Factors/metabolism;叉头转录因子/代谢;Intracellular Signaling Peptides and Proteins/metabolism*;细胞内信号肽类与蛋白质类/代谢*;Mitochondrial Permeability Transition Pore/metabolism*;线粒体通透性转换孔/代谢*;Myocardial Reperfusion Injury/genetics*;心肌再灌注损伤/遗传学*;Myocytes, Cardiac/cytology*;肌细胞,心脏/细胞学*;Nitric Oxide Synthase Type III/metabolism*;一氧化氮合酶III型/代谢*;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;Reactive Oxygen Species/metabolism*;活性氧/代谢*;Repressor Proteins/genetics*;阻遏蛋白质类/遗传学*
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8805992/

编号：18
题名:OEA alleviates apoptosis in diabetic rats with myocardial ischemia/reperfusion injury by regulating the PI3K/Akt signaling pathway through activation of TRPV1.
标题译文:OEA 通过激活 TRPV1 调节 PI3K/Akt 信号通路，减轻糖尿病大鼠心肌缺血/再灌注损伤的细胞凋亡。
作者:Yao, Enhui;Luo, Lili;Lin, Chenxi;Wen, Jing;Li, Yanglongfei;Ren, Tong;Chen, Yujie;Huang, Jinhua;Jin, Xin
出处:Front Pharmacol. 2022-01-01;13:964475.
影响因子:5.6
摘要:Reperfusion therapy after myocardial infarction may lead to myocardial injury, which can be complicated and exacerbated by diabetes. The existing therapeutic methods for myocardial ischemia-reperfusion injury (MIRI) in diabetic patients are not ideal. Oleoylethanolamide (OEA) has been found to have protective effects on diabetes and acute cerebral ischemia. This study aimed to determine whether OEA can alleviate MIRI in diabetic rats, and to explore the underlying mechanism. The model of diabetic rats with MIRI was established by blocking the left coronary artery for 30 min, followed by restoring blood flow stability for 120 min. The myocardial enzyme spectrum, area of MIRI, and expression levels of apoptosis-related proteins were detected. The results showed that OEA pretreatment could reduce myocardial infarction area, protect myocardial tissue structure, and reduce myocardial cell apoptosis in diabetic rats with MIRI. Meanwhile, the levels of creatine kinase (CK)-MB (CK-MB), lactate dehydrogenase (LDH), and malondialdehyde (MDA) were reduced, while superoxide dismutase (SOD) level was elevated. H9C2 cells were treated with high glucose and oxygen-glucose deprivation/reperfusion (OGD/R) to establish an in vitro model. Capsazepine (CPZ), an antagonist of transient receptor potential vanilloid subtype 1 (TRPV1), and LY294002, an inhibitor of PI3K, were used to treat H9C2 cells in vitro. Apoptosis level and the expression levels of apoptosis-related proteins were measured. It was found that OEA activated TRPV1 and the PI3K/Akt signaling pathway, downregulated the expression levels of apoptosis-related proteins (Bcl-2 and cleaved caspase-3), and ameliorated the apoptosis of H9C2 cells treated with high glucose and OGD/R. This study clarified that OEA, as a TRPV1 agonist, could reduce myocardial cell apoptosis by activating

the PI3K/Akt signaling pathway in diabetic rats with MIRI. The findings may provide a theoretical basis for administration of OEA as a potential therapeutic agent into diabetic patients with MIRI.
关键词:oleoylethanolamide, myocardial ischemia-reperfusion injury, diabetic rats, apoptosis, TRPV1
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9701823/

编号：19
题名:Dexmedetomidine promotes cell proliferation and inhibits cell apoptosis by regulating LINC00982 and activating the phosphoinositide-3-kinase (PI3K)/protein kinase B (AKT) signaling in hypoxia/reoxygenation-induced H9c2 cells.
标题译文:Dexmedetomidine 通过调节 LINC00982 和激活缺氧/复氧诱导的 H9c2 细胞中的磷酸肌醇 3 激酶 (PI3K)/蛋白激酶 B (AKT) 信号传导来促进细胞增殖和抑制细胞凋亡。
作者:Wang, Tao;Li, Zhen;Xia, Shuyun;Xu, Zhixin;Chen, Xiaofang;Sun, Hu
出处:BIOENGINEERED. 2022-04-01;13(4):10159-10167.
影响因子:4.9
摘要:Previous studies showed dexmedetomidine (DEX) could alleviate myocardial ischemia/reperfusion injury (MIRI). Nevertheless, the mechanisms by which DEX alleviated MIRI remain to be determined. Our results demonstrated that DEX reversed hypoxia/reoxygenation (H/R)-induced decreased proliferation, and enhanced LINC00982 level, apoptosis, and inflammation in H9c2 cells. Moreover, LINC00982 overexpression attenuated the DEX-mediated protective effect of H9c2 cells under H/R. In addition, DEX upregulated p-phosphoinositide-3-kinase (p-PI3K) and p-protein kinase B (p-AKT) levels, and the silencing of LINC00982 further enhanced this effect in H/R-induced H9c2 cells. Furthermore, LINC00982 deletion enhanced the protective effect of DEX on H9c2 cells under H/R condition, while PI3K inhibitor, LY294002, obviously reversed this phenomenon. In sum, our work determined that DEX could suppress cell apoptosis and inflammation in H/R-triggered H9c2 through downregulating LINC00982 and activating PI3K/AKT signaling.
主题词:Apoptosis/genetics;细胞凋亡/遗传学;Dexmedetomidine*/pharmacology;右美托咪啶*/药理学;Myocardial Reperfusion Injury*;心肌再灌注损伤*;Phosphatidylinositol 3-Kinase;磷脂酰肌醇 3-激酶;Proto-Oncogene Proteins c-akt;原癌基因蛋白质 c-akt
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9161950/

编号：20
题名:The role of PI3K/AKT signaling pathway in myocardial ischemia-reperfusion injury.
标题译文:PI3K/AKT 信号通路在心肌缺血再灌注损伤中的作用
作者:Deng, Rui-Ming;Zhou, Juan
出处:INT IMMUNOPHARMACOL. 2023-10-01;123:110714.

影响因子:4.8
摘要:Myocardial ischemia has a high incidence and mortality rate, and reperfusion is currently the standard intervention. However, reperfusion may lead to further myocardial damage, known as myocardial ischemia/reperfusion injury (MIRI). There are currently no effective clinical treatments for MIRI. The PI3K/Akt signaling pathway is involved in cardiovascular health and disease and plays an important role in reducing myocardial infarct size and restoring cardiac function after MIRI. Activation of the PI3K/Akt pathway provides myocardial protection through synergistic upregulation of antioxidant, anti-inflammatory, and autophagy activities and inhibition of mitochondrial dysfunction and cardiomyocyte apoptosis. Many studies have shown that PI3K/Akt has a significant protective effect against MIRI. Here, we reviewed the molecular regulation of PI3K/Akt in MIRI and summarized the molecular mechanism by which PI3K/Akt affects MIRI, the effects of ischemic preconditioning and ischemic postconditioning, and the role of related drugs or activators targeting PI3K/Akt in MIRI, providing novel insights for the formulation of myocardial protection strategies. This review provides evidence of the role of PI3K/Akt activation in MIRI and supports its use as a therapeutic target.
主题词:Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Phosphatidylinositol 3-Kinases/metabolism;磷脂酰肌醇 3-激酶类/代谢;Myocardial Ischemia*;心肌缺血*
全文链接：
https://newfmrs.metstr.com/search/detail?mid=52c0ffd129b7f3d51944df40aada6173&searchExp=%28The%20role%20of%20PI3K%2FAKT%20signaling%20pathway%20in%20myocardial%20ischemia-reperfusion%20injury%29%20AND%202022%3A2024%5Bdp%5D&needPubmedParse=false&query=%28Th

编号：21
题名:Inhibition of Myocardial Cell Apoptosis Is Important Mechanism for Ginsenoside in the Limitation of Myocardial Ischemia/Reperfusion Injury.
标题译文:抑制心肌细胞凋亡是人参皂苷限制心肌缺血/再灌注损伤的重要机制。
作者:Chen, Zhihan;Wu, Jingping;Li, Sijing;Liu, Caijiao;Ren, Yulan
出处:Front Pharmacol. 2022-01-01;13:806216.
影响因子:5.6
摘要:Ischemic heart disease has a high mortality, and the recommended therapy is reperfusion. Nevertheless, the restoration of blood flow to ischemic tissue leads to further damage, namely, myocardial ischemia/reperfusion injury (MIRI). Apoptosis is an essential pathogenic factor in MIRI, and ginsenosides are effective in inhibiting apoptosis and alleviating MIRI. Here, we reviewed published studies on the anti-apoptotic effects of ginsenosides and their mechanisms of action in improving MIRI. Each ginsenoside can regulate multiple pathways to protect the myocardium. Overall, the involved apoptotic pathways include the death receptor signaling pathway,

mitochondria signaling pathway, PI3K/Akt signaling pathway, NF-κB signaling pathway, and MAPK signaling pathway. Ginsenosides, with diverse chemical structures, regulate different apoptotic pathways to relieve MIRI. Summarizing the effects and mechanisms of ginsenosides contributes to further mechanism research studies and structure-function relationship research studies, which can help the development of new drugs. Therefore, we expect that this review will highlight the importance of ginsenosides in improving MIRI via anti-apoptosis and provide references and suggestions for further research in this field.
关 键 词 :ginsenosides, apoptosis, myocardial ischemia/reperfusion injury, Panax ginseng, review
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8921549/

编号：22
题 名 :L-Borneol 7-O-[β-D-Apiofuranosyl-(1→6)]-β-D-Glucopyranoside Alleviates Myocardial Ischemia-Reperfusion Injury in Rats and Hypoxic/Reoxygenated Injured Myocardial Cells via Regulating the PI3K/AKT/mTOR Signaling Pathway.
标题译文:L-冰片 7-O-[β-D-Apiofuranosyl-(1→6)]-β-D-吡喃葡萄糖苷通过调节 PI3K/AKT/mTOR 信号通路减轻大鼠和缺氧/复氧损伤心肌细胞的心肌缺血再灌注损伤途径。
作者:Tong, Ziyi;Li, Gaowen;Su, Chengxiao;Zhou, Liyan;Zhang, Ling;Chen, Qun;Xia, Qing
出处:J IMMUNOL RES. 2022-01-01;2022:5758303.
影响因子:4.1
摘 要 :Ischemia/reperfusion (I/R) is a primary cause of morbidity and mortality in acute myocardial infarction (AMI). L-Borneol 7-O-[β-D-apiofuranosyl-(1→6)]-β-D-glucopyranoside (LBAG), extracted from the Radix Ophiopogonis, is the main bioactive component that may be exerting cardiovascular protection in AMI. The purpose was to examine the effects of LBAG on myocardial I/R injury (MIRI) in rats and H9c2 cells treated with hypoxia/reoxygenation (H/R). MIRI was induced through the combination of ischemia with reperfusion for 30 min and 24 h, respectively. LBAG was administered 7 days before vascular ligation. Myocardial function was detected by an electrocardiograph, histological, TTC, and TUNEL staining analyses. The influences of LBAG on the content concentration of cardiac enzymes in the serum were measured by ELISA. Moreover, H9c2 cells were exposed to LBAG or combined with AKT inhibitor (perifosine) and then exposed to H/R for simulating the cardiac injury process. Afterward, cell viability, LDH, CD-KM release, apoptosis, and autophagy were evaluated by CCK-8 and ELISA assays, flow cytometry, TUNEL, and immunofluorescence staining, respectively. Additionally, the proteins of apoptosis, autophagy, and PI3K/mTOR pathway were determined by western blotting. In I/R rats, LBAG pretreatment significantly ameliorated cardiac function, as illustrated by reducing the infarct size, myocardial autophagy, and apoptosis levels. In H/R-induced H9c2 cells, LBAG pretreatment significantly decreased cell apoptosis, LC3 II/I, and Beclin 1 levels, elevated the Bcl-2 levels, attenuated LDH, and CD-KM

production. Moreover, LBAG pretreatment markedly increased the PI3K/mTOR pathway activation, and the protective influences of LBAG were partly abolished with the AKT inhibitor perifosine treatment. These findings demonstrated the protective functions of LBAG on I/R by regulating apoptosis and autophagy in vitro and in vivo by activating the PI3K/mTOR pathway.
主题词:Myocardial Infarction*/metabolism;心肌梗塞*/代谢;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Myocardial Reperfusion Injury*/pathology;心肌再灌注损伤*/病理学;Phosphatidylinositol 3-Kinases/metabolism;磷脂酰肌醇3-激酶类/代谢;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质c-akt/代谢;Signal Transduction;信号传导
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9119761/pdf/JIR2022-5758303.pdf

编号：23
题名:Cardiac Protection of a Novel Lupane-Type Triterpenoid from Injuries Induced by Hypoxia-Reperfusion.
标题译文:一种新型羽扇豆型三萜类化合物对缺氧再灌注损伤的心脏保护作用。
作者:Guo, Beibei;Cao, Jiaxin;Liu, Yi;Wang, Yuhang;Qian, Yi;Chen, Guangtong;Zhu, Weizhong
出处:Int J Mol Sci. 2022-08-22;23(16)
影响因子:5.6
摘要:Myocardial ischemia-reperfusion injury (MIRI) leads to cardiac remodeling and heart failure associated with acute myocardial infarction, which is one of the leading causes of death worldwide. Betulinic acid (BA), a widely distributed lupane-type triterpenoid, has been reported to possess antioxidative activity and inhibit apoptosis in MIRI. Due to the low bioavailability and water insolubility of BA, a previous study found a series of BA-derivative compounds by microbial transformation. In this study, we observe whether there are anti-MIRI effects of BTA07, a BA derivative, on cardiac injuries induced by hypoxia/reoxygenation (H/R) in adult rat cardiomyocytes in vitro and in Langendorff-perfused hearts ex vivo, and further explore its mechanism of cardioprotection to find more efficient BA derivatives. The hemodynamic parameters of isolated hearts were monitored and recorded by a Lab Chart system. The markers of oxidative stress and apoptosis in isolated hearts and adult rat cardiomyocytes (ARCMs) were evaluated. The expression levels of B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X (Bax), protein kinase B (Akt) and phospho-Akt (pAkt, Ser473) induced by H/R were detected via Western blot. The Langendorff experiments showed that BTA07 improves hemodynamic parameters, reduces myocardium damage and infarct size, inhibits levels of myocardial tissue enzymes lactate dehydrogenase (LDH) and creatine kinase (CK) in the coronary outflow and reduces oxidative stress and the activation of caspase-3 in the myocardium. In vitro, BTA07 reduced cell death and caspase-3 activation and inhibited reactive oxygen species (ROS) generation. Furthermore, the protective effects of BTA07 were

attenuated by inhibition of the PI3K/Akt signaling pathway with LY294002 in ARCMs. BTA07 protects ARCMs and isolated hearts from hypoxia-reperfusion partly by inhibiting oxidative stress and cardiomyocyte apoptosis.
主题词:Apoptosis;细胞凋亡;Cardiotonic Agents*/pharmacology;强心药*/药理学;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Pentacyclic Triterpenes*/pharmacology;五环三萜类*/药理学;Phosphatidylinositol 3-Kinases/metabolism;磷脂酰肌醇3-激酶类/代谢;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9409286/

编号：24
题名:Long non-coding RNA MALAT1 modulates myocardial ischemia-reperfusion injury through the PI3K/Akt/eNOS pathway by sponging miRNA-133a-3p to target IGF1R expression.
标题译文:长链非编码 RNA MALAT1 通过 PI3K/Akt/eNOS 通路调节心肌缺血再灌注损伤，通过海绵 miRNA-133a-3p 靶向 IGF1R 表达。
作者:Liu, Xin-Ming;Zhang, Zhenzhou;Zhong, Jiuchang;Li, Ning;Wang, Tao;Wang, Lefeng;Zhang, Qian
出处:EUR J PHARMACOL. 2022-02-05;916:174719.
影响因子:5.0
摘要:The mechanism of myocardial ischemia-reperfusion injury (MIRI) is a complex pathophysiological process that can lead to poor patient outcomes. Although LncRNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is reported to be highly expressed in myocardial ischemia reperfusion (IR) injury, the specific mechanism remains largely unknown. This study aimed to elucidate the roles and possible mechanism of MALAT1 in myocardial IR injury. IR model was established in rats by ligation of the anterior descending artery in vivo, and H9c2 and HL-1 cells were treated by hypoxia/reoxygenation (HR) to construct the model in vitro. The small interfering RNA (siRNA) for MALAT1 and miR-133a-3p mimics, inhibitor was used to transfect the cells. The expression of MALAT1, miR-133a-3p in MIRI were evaluated using real-time quantitative polymerase chain reaction (qRT-PCR), immunohistochemistry (IHC) and western blot (WB). Relationships between MALAT1, insulin-like growth factor 1 receptor (IGF1R) with miR-133a-3p were confirmed by luciferase reporter assay. Annexin V-FITC/PI double-labeled flow cytometry, terminal dexynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL), Cell Counting Kit-8 (CCK-8), serum creatine kinase MB (CK-MB), and lactate dehydrogenase (LDH) were evaluated to examine the impact of MALAT1 on MIRI. Our results revealed that MALAT1 was highly expressed, while miR-133a-3p and IGF1R were repressed in IR and HR groups. Knockdown of MALAT1 alleviate the pro-apoptotic effect and myocardial injury in vitro and in vivo. Systematically, MALAT1 may serve as a sponge for miR-133a-3p to suppress IGF1R, which a direct target of miR-133a-3p, then inhibit the PI3K/Akt/eNOS survival pathway. Mechanistically, our study demonstrated that MALAT1 regulates PI3K/Akt/eNOS

signaling via miR-133a-3p. In summary, these results suggest that MALAT1 and miR-133a-3p play important roles in MIRI. MALAT1 regulates miR-133a-3p /IGF1R axis. These results show light on the underlying mechanisms of MIRI and provide potential therapeutic targets for MIRI.
主题词:Apoptosis/genetics;细胞凋亡/遗传学;MicroRNAs*/genetics;微 RNAs*/遗传学 ;MicroRNAs*/metabolism; 微 RNAs*/ 代 谢 ;Myocardial Reperfusion Injury*/metabolism; 心 肌 再 灌 注 损 伤 */ 代 谢 ;Phosphatidylinositol 3-Kinases/metabolism; 磷 脂 酰 肌 醇 3- 激 酶 类 / 代 谢 ;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;RNA, Long Noncoding*/genetics;RNA, 长链非编码*/遗传学;RNA, Long Noncoding*/metabolism;RNA, 长链非编码*/代谢
全文链接：
https://newfmrs.metstr.com/search/detail?mid=50c495ba4f31e2e9ad7710b45d0ef5be&searchExp=%28Long%20non-coding%20RNA%20MALAT1%20modulates%20myocardial%20ischemia-reperfusion%20injury%20through%20the%20PI3K%2FAkt%2FeNOS%20pathway%20by%20sponging%20miRNA-133a-

编号：25
题名:Hydromorphone hydrochloride preconditioning combined with postconditioning attenuates myocardial ischemia/reperfusion injury in rats by improving mitochondrial function and activating the PI3K/Akt signaling pathway.
标题译文:盐酸氢吗啡酮预处理联合后处理通过改善线粒体功能和激活 PI3K/Akt 信号通路减轻大鼠心肌缺血/再灌注损伤。
作 者 :Qiu, Liuji;Yan, Yan;Zhong, Guocheng;Hou, Zhiqi;Ye, Yongcai;Lin, Jiaying;Luo, Dexing
出处:CHEM BIOL DRUG DES. 2024-02-01;103(2):e14474.
影响因子:3.2
摘 要 :Thrombolytic therapy or percutaneous coronary intervention for myocardial infarction often cause myocardial ischemia/reperfusion injury (MIRI) and poor prognosis of patients. This study aimed to explore the protective effect and potential mechanism of hydromorphone hydrochloride (HH) on MIRI. Fifty Sprague-Dawley male rats were randomly divided into Sham group, I/R group, HH-pre group, HH-post group, and HH-pre + post group. Except Sham group, MIRI models were established by ligating and relaxing the left anterior descending coronary artery, followed by tail vein injection of HH (0.3 μmol/L) 10 min before ligation (HH-pre group), 10 min after reperfusion (HH-post group), and twice at the above two time points (HH-pre + post group). After intervention, the cardiac function of rats was evaluated by echocardiography, and the levels of myocardial injury markers, oxidative stress indicators, and mitochondrial function indicators were detected. Next, the myocardial infarction area was evaluated by 2,3,5-triphenyltetrazolium chloride staining, mitochondrial biogenesis, and phosphoinositide 3 kinase (PI3K)/protein kinase B (Akt) signaling pathway by western blot. Compared with the I/R group, HH intervention improved cardiac function, decreased myocardial infarction area, reduced serum

myocardial injury markers, alleviated oxidative stress, improved mitochondrial function, up-regulated mitochondrial biogenesis, and activated PI3K/Akt signaling pathway. Moreover, the HH-pre + post group was superior to the HH-pre and HH-post groups in the above aspects. Collectively, HH had protective effect on MIRI rats, and HH preconditioning combined with postconditioning showed optimal efficacy. Such efficacy may be achieved by promoting mitochondrial biogenesis to improve mitochondrial function and reduce oxidative stress, and activating the PI3K/Akt signaling pathway.
主题词:Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Myocardial Infarction*/drug therapy;心肌梗塞*/药物疗法
全文链接：
https://newfmrs.metstr.com/search/detail?mid=edb03f08288b905e290fb233b856d0ee&searchExp=%28Hydromorphone%20hydrochloride%20preconditioning%20combined%20with%20postconditioning%20attenuates%20myocardial%20ischemia%2Freperfusion%20injury%20in%20rats%20by%20i

编号：26
题名:Natural Products Targeting PI3K/AKT in Myocardial Ischemic Reperfusion Injury: A Scoping Review.
标题译文:针对心肌缺血再灌注损伤中的 PI3K/AKT 的天然产物：范围综述。
作者:Syed Abd Halim, Syarifah Aisyah;Abd Rashid, Norhashima;Woon, Choy Ker;Abdul Jalil, Nahdia Afiifah
出处:Pharmaceuticals (Basel). 2023-05-12;16(5)
影响因子:4.3
摘要:This scoping review aimed to summarize the effects of natural products targeting phosphoinositide-3-kinases/serine/threonine kinase (PI3K/AKT) in myocardial ischemia-reperfusion injury (MIRI). The review details various types of natural compounds such as gypenoside (GP), gypenoside XVII (GP-17), geniposide, berberine, dihydroquercetin (DHQ), and tilianin which identified to reduce MIRI in vitro and in vivo by regulating the PI3K/AKT signaling pathway. In this study, 14 research publications that met the inclusion criteria and exclusion criteria were shortlisted. Following the intervention, we discovered that natural products effectively improved cardiac functions through regulation of antioxidant status, down-regulation of Bax, and up-regulation of Bcl-2 and caspases cleavage. Furthermore, although comparing outcomes can be challenging due to the heterogeneity in the study model, the results we assembled here were consistent, giving us confidence in the intervention's efficacy. We also discussed if MIRI is associated with multiple pathological condition such as oxidative stress, ERS, mitochondrial injury, inflammation, and apoptosis. This brief review provides evidence to support the huge potential of natural products used in the treatment of MIRI due to their various biological activities and drug-like properties.

关 键 词 :medicinal plants, PI3K/AKT, myocardial ischemic reperfusion injury, phytochemicals, cardiovascular disease
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10221447/

编号：27
题 名 :Natural compounds regulate the PI3K/Akt/GSK3β pathway in myocardial ischemia-reperfusion injury.
标题译文:天然化合物调节心肌缺血再灌注损伤中的 PI3K/Akt/GSK3β 通路。
作 者 :Ajzashokouhi, Amir Hossein;Rezaee, Ramin;Omidkhoda, Navid;Karimi, Gholamreza
出处:CELL CYCLE. 2023-04-01;22(7):741-757.
影响因子:3.4
摘 要 :The PI3K/Akt/GSK3β pathway is crucial in regulating cardiomyocyte growth and survival. It has been shown that activation of this pathway alleviates the negative impact of ischemia-reperfusion. Glycogen synthase kinase-3 (GSK3β) induces apoptosis through stimulation of transcription factors, and its phosphorylation has been suggested as a new therapeutic target for myocardial ischemia-reperfusion injury (MIRI). GSK3β regulatory role is mediated by the reperfusion injury salvage kinase (RISK) pathway, and its inhibition by Akt activation blocks mitochondrial permeability transition pore (mPTP) opening and enhances myocardial survival. The present article discusses the involvement of the PI3K/Akt/GSK3β pathway in cardioprotective effects of natural products against MIRI.Abbreviations: Akt: protein kinase B; AMPK: AMP-activated protein kinase; ATP: adenosine triphosphate; Bad: bcl2-associated agonist of cell death; Bax: bcl2-associated x protein; Bcl-2: B-cell lymphoma 2; CK-MB: Creatine kinase-MB; CRP: C-reactive-protein; cTnI: cardiac troponin I; EGCG: Epigallocatechin-3-gallate; Enos: endothelial nitric oxide synthase; ER: endoplasmic reticulum; ERK ½: extracellular signal-regulated protein kinase ½; GSK3β: glycogen synthase kinase-3; GSRd: Ginsenoside Rd; GSH: glutathione; GSSG: glutathione disulfide; HO-1: heme oxygenase-1; HR: hypoxia/reoxygenation; HSYA: Hydroxysafflor Yellow A; ICAM-1: Intercellular Adhesion Molecule 1; IKK-b: IκB kinase; IL: interleukin; IPoC: Ischemic postconditioning; IRI: ischemia-reperfusion injury; JNK: c-Jun N-terminal kinase; Keap1: kelch-like ECH-associated protein- 1; LDH: lactate dehydrogenase; LVEDP: left ventricular end diastolic pressure; LVP: left ventricle pressure; LVSP: left ventricular systolic pressure; MAPK: mitogen-activated protein kinase; MDA: malondialdehyde; MIRI: myocardial ischemia-reperfusion injury; MnSOD: manganese superoxide dismutase; mPTP: mitochondrial permeability transition pore; mtHKII: mitochondria-bound hexokinase II; Nrf-1: nuclear respiratory factor 1; Nrf2: nuclear factor erythroid 2-related factor; NO: nitric oxide; PGC-1α: peroxisome proliferator-activated receptor γ coactivator-1α; PI3K: phosphoinositide 3-kinases; RISK: reperfusion injury salvage kinase; ROS: reactive oxygen species; RSV: Resveratrol; SOD: superoxide dismutase; TFAM: transcription factor A mitochondrial; TNF-α: tumor necrosis factor-alpha; VEGF-B: vascular endothelial growth factor B.

主题词:Proto-Oncogene Proteins c-akt*/metabolism;原癌基因蛋白质 c-akt*/代谢;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Phosphatidylinositol 3-Kinases/metabolism;磷脂酰肌醇 3-激酶类/代谢
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10026916/

编号：28
题名:Mild therapeutic hypothermic protection activates the PI3K/AKT signaling pathway to inhibit TRPM7 and suppress ferroptosis induced by myocardial ischemia-reperfusion injury.
标题译文:轻度治疗性低温保护可激活 PI3K/AKT 信号通路，抑制 TRPM7 并抑制心肌缺血再灌注损伤引起的铁死亡。
作者:Li, Yaqi;Chen, Yixuan;Yu, Peng;Zhang, Deju;Tang, Xiaoyi;Zhu, Zicheng;Xiao, Fan;Deng, Wei;Liu, Yang;Tan, Zhaoying;Zhang, Jing;Yu, Shuchun
出处:MOL MED REP. 2024-12-01;30(6)
影响因子:3.4
摘要:The present study aimed to investigate the role of PI3K-mediated ferroptosis signaling induced by mild therapeutic hypothermia (MTH), which was defined as a temperature of 34˚C, in protecting against myocardial ischemia-reperfusion (I/R) injury (MIRI). To meet this aim, H9C2 cells underwent hypoxia-reperfusion (H/R) and/or MTH. The MTT assay was used to assess cell viability, cytotoxicity was measured using a lactate dehydrogenase cytotoxicity assay, and Annexin V-FITC/PI flow cytometric analysis was used to analyze early and late cell apoptosis. In addition, 84 healthy adult male Sprague-Dawley rats were randomly divided into seven groups (n=12), and underwent I/R and various treatments. Hemodynamics were monitored, and the levels of myocardial injury marker enzymes and oxidative stress markers in myocardial tissue were measured using ELISA. The expression levels of PI3K, AKT, transient receptor potential cation channel subfamily M member 7 (TRPM7), glutathione peroxidase 4 (GPX4) and acyl-CoA synthetase long chain family member 4 (ACSL4) in animals and cells were measured using western blot analysis. These experiments revealed that MTH could effectively reduce myocardial infarct size, improve hemodynamic performance following MIRI and suppress myocardial apoptosis, thereby contributing to the recovery from H/R injury. Mechanistically, MTH was revealed to be able to activate the PI3K/AKT signaling pathway in cells, upregulating GPX4, and downregulating the expression levels of TRPM7 and ACSL4. Treatment with 2-aminoethoxydiphenyl borate (an inhibitor of TRPM7) could further strengthen the myocardial protective effects of MTH, whereas treatment with erastin (promoter of ferroptosis) and wortmannin (inhibitor of PI3K) led to the effective elimination of the myocardial protective effects of MTH. Compared with in the I/R group, the PI3K/AKT activation level and the expression levels of GPX4 were both significantly increased, whereas the expression levels of TRPM7 and ACSL4 were significantly decreased in the I/R + MTH group. Taken together, the results of the present study indicated that MTH may activate the PI3K/AKT signaling pathway to inhibit TRPM7 and suppress ferroptosis induced by MIRI.

主题词:Ferroptosis*/drug effects;铁死亡*/药物作用;TRPM Cation Channels*/metabolism;TRPM 阳离子通道*/代谢;TRPM Cation Channels*/antagonists & inhibitors;TRPM 阳离子通道*/拮抗剂与抑制剂;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Signal Transduction*/drug effects;信号传导*/药物作用;Phosphatidylinositol 3-Kinases*/metabolism;磷脂酰肌醇3-激酶类*/代谢;Proto-Oncogene Proteins c-akt*/metabolism;原癌基因蛋白质c-akt*/代谢;Rats, Sprague-Dawley*;大鼠,Sprague-Dawley*
全文链接:
https://newfmrs.metstr.com/search/detail?mid=80f70648dc111fd5a91dba1cf48c92d0&searchExp=%28Mild%20therapeutic%20hypothermic%20protection%20activates%20the%20PI3K%2FAKT%20signaling%20pathway%20to%20inhibit%20TRPM7%20and%20suppress%20ferroptosis%20induced%20

编号:29
题名:Plantamajoside alleviates hypoxia-reoxygenation injury through integrin-linked kinase/c-Src/Akt and the mitochondrial apoptosis signaling pathways in H9c2 myocardial cells.
标题译文:Plantamajoside 通过整合素连接激酶/c-Src/Akt 和线粒体凋亡信号通路减轻 H9c2 心肌细胞的缺氧复氧损伤。
作者:Du, Yuying;Li, Jia;Cai, Chao;Gong, Fanying;Zhou, Guoliang;Liu, Fang;Wu, Qiang;Liu, Fuming
出处:BMC Complement Med Ther. 2023-02-24;23(1):64.
影响因子:3.3
摘要:Myocardial ischemia-reperfusion injury(MIRI) is one of the common complications after myocardial infarction surgery, Oxidative stress is among the main mechanisms of myocardial ischemia-reperfusion injury. Plantamajoside (PMS), the main effective ingredient in the genus Plantain, has been reported to possess an antioxidation, anti-inflammatory and anti-apoptosis role. However, whether PMS can attenuate myocardial ischemia-reperfusion injury is not yet known. Herein, we explored the effects of PMS on hypoxia-reoxygenation (H/R) injury in H9c2 cardiomyocytes and the underling molecular mechanisms of the treatment. Network pharmacological analysis screened the top 31 key genes in the treatment of MIRI disease treated with PMS, and the result of molecular docking further illustrated the roles that the PMS play in the treatment of MIRI through its interference with integrin-linked kinase (ILK) target protein. PMS was not cytotoxic in the concentration range of 5-40 μM and increased cell survival after H/R injury in a concentration-dependent manner without affecting proliferation or growth. PMS significantly reduced the levels of lactate dehydrogenase, malonic dialdehyde, reactive oxygen species and cell apoptosis, and increased soperoxide dismutase activity compared with those of the H/R injury group. PMS promoted the protein and mRNA expression of ILK and Bcl-2, the protein expression of p-Akt, and reduced the

protein and mRNA expression of Bax, Caspase-3, and Cytochrome c, the protein expression of p-c-Src. PMS has protective effects against H/R injury in H9c2 cells, and its protective mechanism may be related to reactive oxygen species clearance, activation of the ILK/c-Src/Akt pathway and inhibition of the mitochondrial apoptosis.
主题词:Proto-Oncogene Proteins c-akt*/metabolism;原癌基因蛋白质 c-akt*/代谢;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Signal Transduction;信号传导
全文链接：https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9951442/

编号：30
题名:Myocardial ischemia-reperfusion injury is probably due to the excessive production of mitochondrial ROS caused by the activation of 5-HT degradation system mediated by PAF receptor.
标题译文:心肌缺血再灌注损伤可能是由于 PAF 受体介导的 5-HT 降解系统激活导致线粒体 ROS 产生过多所致。
作者:Jin, Jiaqi;Xu, Fan;Zhang, Yuxin;Guan, Jing;Fu, Jihua
出处:MOL IMMUNOL. 2023-03-01;155:27-43.
影响因子:3.2
摘要:AIM:Previously, we revealed a crucial role of 5-HT degradation system (5DS), consisting of 5-HT2A receptor (5-HT2AR), 5-HT synthases and monoamine oxidase A (MAO-A), in ischemia-reperfusion (IR)-caused organ injury. Whereas, platelet activating factor receptor (PAFR) also mediates myocardial ischemia-reperfusion injury (MIRI). Here, we try to clarify the relationship between 5DS and PAFR in mediating MIRI.METHODS:H9c2 cell injury and rat MIRI were caused by hypoxia/reoxygenation (H/R) or PAF, and by ligating the left anterior descending coronary artery then untying, respectively. 5-HT2AR and PAFR antagonists [sarpogrelate hydrochloride (SH) and BN52021], MAO-A, AKT, mTOR and 5-HT synthase inhibitors (clorgyline, perifosine, rapamycin and carbidopa), and gene-silencing PKCε were used in experiments RESULTS: The mitochondrial ROS production, respiratory chain damage, inflammation, apoptosis and myocardial infarction were significantly prevented by BN52021, SH and clorgyline in H/R and PAF-treated cells and in IR myocardium. BN52021 also significantly suppressed the upregulation of PAFR, 5-HT2AR, 5-HT synthases and MAO-A expression (mRNA and protein), and Gαq and PKCε (in plasmalemma) expression induced by H/R, PAF or IR; the effects of SH were similar to that of BN52021 except for no affecting the expression of PAFR and 5-HT2AR. Gene-silencing PKCε suppressed H/R and PAF-induced upregulation of 5-HT synthases and MAO-A expression in cells; perifosine and rapamycin had not such effects; however, clorgyline suppressed H/R and PAF-induced phosphorylation of AKT and mTOR.CONCLUSION:MIRI is probably due to PAFR-mediated 5-HT2AR activation, which further activates PKCε-mediated 5-HT synthesis and degradation, leading to mitochondrial ROS production.
主题词:Apoptosis;细胞凋亡;Clorgyline/pharmacology;氯吉兰/药理学;Monoamine

Oxidase/pharmacology; 单胺氧化酶/药理学;Myocardial Reperfusion Injury*/metabolism; 心肌再灌注损伤*/代谢;Platelet Membrane Glycoproteins*/metabolism;血小板膜糖蛋白类*/代谢;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;Reactive Oxygen Species*/metabolism; 活性氧*/代谢;Reactive Oxygen Species*/toxicity;活性氧*/毒性;Receptors, G-Protein-Coupled*/metabolism;受体, G-蛋白偶联*/代谢;Serotonin*/metabolism;血清素*/代谢;Serotonin*/pharmacology;血清素*/药理学
全文链接：
https://newfmrs.metstr.com/search/detail?mid=5bfe340aa537040cdfd792ed311e926e&searchExp=%28Myocardial%20ischemia-reperfusion%20injury%20is%20probably%20due%20to%20the%20excessive%20production%20of%20mitochondrial%20ROS%20caused%20by%20the%20activation%20of

编号：31
题名:Tongxinluo Activates PI3K/AKT Signaling Pathway to Inhibit Endothelial Mesenchymal Transition and Attenuate Myocardial Fibrosis after Ischemia-Reperfusion in Mice.
标题译文:通心络激活 PI3K/AKT 信号通路抑制内皮间质转化并减轻小鼠缺血再灌注后的心肌纤维化。
作者:Wei, Ya-Ru;Hou, Yun-Long;Yin, Yu-Jie;Li, Zhen;Liu, Yi;Han, Ning-Xin;Wang, Zi-Xuan;Liu, Lu;Wang, Xiao-Qi;Hao, Yuan-Jie;Ma, Kun;Gu, Jiao-Jiao;Jia, Zhen-Hua
出处:CHIN J INTEGR MED. 2024-07-01;30(7):608-615.
影响因子:2.2
摘要:OBJECTIVE:To investigate the potential role of Tongxinluo (TXL) in attenuating myocardial fibrosis after myocardial ischemia-reperfusion injury (MIRI) in mice.METHODS:A MIRI mouse model was established by left anterior descending coronary artery ligation for 45 min. According to a random number table, 66 mice were randomly divided into 6 groups (n=11 per group): the sham group, the model group, the LY-294002 group, the TXL group, the TXL+LY-294002 group and the benazepril (BNPL) group. The day after modeling, TXL and BNPL were administered by gavage. Intraperitoneal injection of LY-294002 was performed twice a week for 4 consecutive weeks. Echocardiography was used to measure cardiac function in mice. Masson staining was used to evaluate the degree of myocardial fibrosis in mice. Qualitative and quantitative analysis of endothelial mesenchymal transition (EndMT) after MIRI was performed by immunohistochemistry, immunofluorescence staining and flow cytometry, respectively. The protein expressions of platelet endothelial cell adhesion molecule-1 (CD31), α-smoth muscle actin (α-SMA), phosphatidylinositol-3-kinase (PI3K) and phospho protein kinase B (p-AKT) were assessed using Western blot.RESULTS:TXL improved cardiac function in MIRI mice, reduced the degree of myocardial fibrosis, increased the expression of CD31 and inhibited the expression of α-SMA, thus inhibited the occurrence of EndMT ($P<0.05$ or $P<0.01$). TXL significantly increased the protein

expressions of PI3K and p-AKT (P<0.05 or P<0.01). There was no significant difference between TXL and BNPL group (P>0.05). In addition, the use of the PI3K/AKT pathway-specific inhibitor LY-294002 to block this pathway and combination with TXL intervention, eliminated the protective effect of TXL, further supporting the protective effect of TXL.CONCLUSION:TXL activated the PI3K/AKT signaling pathway to inhibit EndMT and attenuated myocardial fibrosis after MIRI in mice.
主题词:Drugs, Chinese Herbal*/pharmacology;中草药*/药理学;Drugs, Chinese Herbal*/therapeutic use;中草药*/治疗应用;Proto-Oncogene Proteins c-akt*/metabolism;原癌基因蛋白质c-akt*/代谢;Phosphatidylinositol 3-Kinases*/metabolism;磷脂酰肌醇3-激酶类*/代谢;Signal Transduction*/drug effects;信号传导*/药物作用;Fibrosis*;纤维化*;Myocardial Reperfusion Injury*/drug therapy;心肌再灌注损伤*/药物疗法;Myocardial Reperfusion Injury*/pathology;心肌再灌注损伤*/病理学;Myocardium*/pathology;心肌*/病理学
全文链接：
https://newfmrs.metstr.com/search/detail?mid=797c71ffeb51b477fa165b618c462602&searchExp=%28Tongxinluo%20Activates%20PI3K%2FAKT%20Signaling%20Pathway%20to%20Inhibit%20Endothelial%20Mesenchymal%20Transition%20and%20Attenuate%20Myocardial%20Fibrosis%20after%2

编号：32
题名:Total saponins of Aralia elata (Miq.) Seem. alleviate myocardial ischemia-reperfusion injury by promoting NLRP3-inflammasome inactivation via PI3K/Akt signaling.
标题译文:Aralia elata (Miq.) Seem 的总皂苷。 通过 PI3K/Akt 信号促进 NLRP3 炎性体失活来减轻心肌缺血再灌注损伤。
作者:Sun, Li;Lu, Wei-Xing;Li, Hui;Feng, Ding-Ya;Nie, Jing-Xiao
出处:KAOHSIUNG J MED SCI. 2023-03-01;39(3):290-301.
影响因子:2.7
摘要:Total saponins of Aralia elata (Miq.) Seem. (TSAE) have been shown to play a significant role in cardiovascular protection, anti-tumor, liver protection, anti-oxidant stress, and anti-inflammation. However, the specific mechanisms of TSAE in myocardial ischemia-reperfusion injury (MIRI) remain largely elusive. Hearts from male Wistar rats were used to establish the isolated heart MIRI model. Using a multichannel physiological recorder, the whole course heart rate (HR), left ventricular development pressure (LVDP), and maximum rise/decrease rate of left ventricular pressure (±dp/dtmax) were recorded. 2,3,5-triphenyl-2H-tetrazolium chloride staining observed the infarct area, while hematoxylin & eosin staining detected pathological changes in myocardial tissue. Creatine kinase, lactate dehydrogenase, total superoxide dismutase, and malondialdehyde concentrations were determined by enzyme-linked immunosorbent assay. Immunohistochemistry, quantitative PCR, and western blot assay were used to assess the amounts of IL-18 and IL-1β, NLR family protein (NLRP3) inflammasome- and apoptosis-related proteins, respectively. Treatment with

TSAE or MCC950 (NLRP3-specific inhibitor) significantly reduced the myocardial infarction area, alleviated pathological changes in myocardial tissues, enhanced LVDP and ±dp/dtmax levels, prevented myocardial oxidative damage, and inhibited NLRP3 inflammasome formation. In addition, TSAE enhanced Akt and GSK3β phosphorylation, and LY29004 co-reperfusion markedly diminished the protective role of TSAE reperfusion on cardiac function, oxidative damage, and inflammatory responses. Collectively, TSAE treatment exhibited a protective effect on I/R-triggered inflammatory responses, cell necrosis, and oxidative stress injury by stimulating PI3K/Akt signaling-mediated NLRP3 inflammasome inhibition.

主题词:Proto-Oncogene Proteins c-akt/genetics;原癌基因蛋白质 c-akt/遗传学;Proto-Oncogene Proteins c-akt/metabolism;原癌基因蛋白质 c-akt/代谢;Aralia*/metabolism;楤木属*/代谢;Phosphatidylinositol 3-Kinases/metabolism;磷脂酰肌醇 3-激酶类/代谢;Myocardial Reperfusion Injury*/metabolism;心肌再灌注损伤*/代谢;Saponins*/pharmacology;皂苷类*/药理学;Saponins*/therapeutic use;皂苷类*/治疗应用;Apoptosis;细胞凋亡

全文链接：

https://newfmrs.metstr.com/search/detail?mid=7c925cc6427a9d41a5bedd29e23f5a4b&searchExp=%28Total%20saponins%20of%20Aralia%20elata%20%28Miq.%29%20Seem.%20alleviate%20myocardial%20ischemia-reperfusion%20injury%20by%20promoting%20NLRP3-inflammasome%20inactiva