Journal of
Kerman University of Medical Sciences

https://jkmu.kmu.ac.ir
doi:10.34172/jkmu.4052
JKMU 2026;33:4052

Review Article

Open Access
Publish Free

MG53 as a Potential Therapeutic Target for Myocardial Infarction Injury

Zeinab Farhadi[1,3], Mansour Esmailidehaj[1], Fatemeh Zare Mehrjardi[1], Hossein Azizian[1,2*]

[1]Yazd Neuroendocrine Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[2]Reproductive Immunology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[3]Stem Cell Biology Research Center, Yazd Reproductive Sciences Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

***Corresponding Author:** Hossein Azizian, Email: H.azizian@ssu.ac.ir

Abstract

Introduction: Myocardial infarction (MI) leads to irreversible cardiomyocyte loss and progressive ventricular remodeling largely driven by oxidative stress, inflammation, and mitochondrial dysfunction. Mitsugumin 53 (MG53/TRIM72) is a muscle-enriched membrane-repair protein that has emerged as a multifunctional regulator of cellular antioxidant responses, mitochondrial integrity, and anti-inflammatory signaling. This review synthesizes current evidence on the MG53's mechanisms and therapeutic potential in MI.

Methods: We performed a narrative review of preclinical and translational literature focusing on MG53 in cardiac injury. Databases searched included PubMed and Google Scholar (through 2025), using keywords "MG53," "TRIM72," "myocardial infarction," "ischemia-reperfusion," "recombinant MG53," and "cardioprotection." Relevant mechanistic studies, recombinant protein interventions, and reports on the MG53's systemic effects and safety were prioritized.

Results: Preclinical studies demonstrate that MG53 promotes plasma-membrane resealing, preserves mitochondrial membrane potential, reduces mitochondrial ROS production, attenuates mitophagy, and upregulates endogenous antioxidant enzymes (e.g., HO-1, catalase, SOD). Recombinant human MG53 (rhMG53) or MG53 overexpression reduces infarct size, limits cardiomyocyte apoptosis, and improves functional recovery in rodent ischemia–reperfusion models. Additional benefits include suppression of NF-κB–mediated inflammation and modulation of necroptotic pathways via RIPK1 ubiquitination. However, there are conflicting data: chronic MG53 upregulation in some models has been associated with insulin signaling perturbation, and human data remain limited with variable reports on the cardiac MG53 expression and circulating levels. Safety, pharmacokinetics, and optimal delivery strategies for rhMG53 require further characterization.

Conclusion: MG53 represents a promising cardioprotective target for MI through multimodal actions on membrane repair, mitochondrial protection, and antioxidant gene regulation. Translation to clinical therapy will require rigorous preclinical safety profiling, clarification of MG53's systemic metabolic effects, and well-designed early-phase studies to evaluate pharmacology, dosing, and efficacy in humans. Future studies should explicitly address human expression patterns and reconcile metabolic concerns to safely harness MG53-based interventions.

Keywords: MG53 protein, Myocardial infarction, Oxidative stress, Cardiovascular diseases

Citation: Farhadi Z, Esmailidehaj M, Zare Mehrjardi F, Azizian H. MG53 as a potential therapeutic target for myocardial infarction injury. Journal of Kerman University of Medical Sciences 2026;33:4052. doi:10.34172/jkmu.4052

Received: September 29, 2025, **Accepted**: November 12, 2025, **ePublished**: May 3, 2026

Introduction

Myocardial infarction (MI) injury constitutes a sudden impairment that often leads to permanent disabilities and disruptions of muscle and cardiovascular functions (1). According to the World Health Organization (WHO), cardiovascular diseases are the leading cause of death globally, accounting for an estimated 19.8 million deaths each year, of which more than 85% are due to heart attack and stroke. Beyond mortality, MI imposes a substantial economic burden on healthcare systems and society, including the costs of acute treatment, long-term care, and rehabilitation. Furthermore, survivors of MI often experience a significant reduction in quality of life due to chronic heart failure, recurrent hospitalizations, and physical limitations, which collectively underscore the global impact of this condition (2, 3). MI injury occurs in two stages: initial ischemic injury can cause direct harm to the structure of cardiomyocytes, while mechanical tissue deformation triggers secondary injury, resulting in ventricular wall damage, edema, increased cardiac load, inflammation, and cellular death (4). This secondary injury represents the progression of MI and serves as the catalyst for long-term physical and functional cardiac changes, often resulting in permanent disability for affected individuals (5, 6). The secondary injury is primarily caused by oxidative stress, which leads to cardioinflammation, damages cardiomyocytes, promotes cell death, and ultimately results in chronic heart failure in MI cases (7). There are complex

relationships between MI, inflammation, and oxidative stress (8). Following cardiac ischemia, multiple pro-inflammatory factors are released into the bloodstream. These include interleukin-1 beta (IL-1β), interleukin-6 (IL-6), interferon gamma (IFN-γ), tumor necrosis factor alpha (TNF-α), plasminogen activator inhibitor-1, and transforming growth factor beta (TGF-β). Their combined activity exacerbates the ischemic condition of the heart by promoting oxidative stress (9, 10). Previous reports indicated a strong correlation between oxidative stress and these factors, highlighting oxidative stress itself as a factor that exacerbates the production of inflammatory cytokines (11). It has been shown that oxidative stress triggers inflammatory cascades through the activation of monocyte chemoattractant protein-1 (MCP-1), TNF-α, IL-1β, and IL-6, resulting in cardiovascular complications following MI (10, 12). Additionally, oxidative stress activates matrix metalloproteinases (MMPs) that degrade gap junction proteins, leading to cardiomyocyte damage in MI, and likely contributing to cardiovascular disparities in MI patients (13). Oxidative stress is recognized as one of the initiators of cell death following cardiac injury (14) and is generated at high levels in MI hearts and stimulates cellular death (15). The predominant cell death process in the secondary injury of MI is apoptosis, a form of programmed cell death triggered by the activation of caspase enzymes (16). The Mitsoguminin 53 (MG53) protein, a member of the tripartite motif (TRIM) family, plays a crucial role in protecting against various pathological conditions by inhibiting inflammation and apoptosis, promoting tissue regeneration and repair, repairing cell membrane damage, and modulating detoxification processes (17). Additionally, MG53 enhances antioxidant capacity by upregulating the expression of antioxidant genes such as heme oxygenase-1 (HO-1), catalase, superoxide dismutase (SOD), and nicotinamide adenine dinucleotide phosphate (NADPH) oxidoreductases (18, 19). Given these functions, MG53 shows promise as a therapeutic agent for mitigating cardiac damage resulting from cardiovascular injury. This analysis explores the role of oxidative stress in MI pathogenesis and the potential of targeting the antioxidant signaling pathway of MG53 to alleviate MI-induced oxidative damage.

Methods

Strategy

A structured approach for identifying all of the preclinical and translational literature focusing on MG53 in cardiac injury.

- Databases: PubMed and Google Scholar (through 2025)
- Keywords: MG53, TRIM72, myocardial infarction, ischemia-reperfusion, recombinant MG53, and cardioprotection
- Filters: Relevant mechanistic studies, recombinant protein interventions, and reports on MG53's systemic effects and safety were prioritized.

Study Selection

- Title and abstract screening by at least two independent reviewers
- Full-text review of potentially eligible studies
- Disagreements between reviewers regarding study eligibility or data extraction were resolved through discussion and consensus. If consensus could not be reached, a third reviewer was consulted to make the final decision.

Data Extraction

- Author(s), year of publication
- Study design and setting
- Population characteristics (e.g., sample size, age, sex)
- Interventions (if applicable)
- Outcomes measured
- Main findings and conclusions

Critical Appraisal

- To ensure that only high-quality evidence informs conclusions
- To assess the internal validity and applicability of each study's findings

Results

Oxidative Stress as the Major Source of Cardiopathology in MI

Oxidative stress stands out as the primary contributor to the secondary injury of MI, characterized by an imbalance between oxidants and antioxidants, which subjects cells to biochemical and physiological damage (20). Free radicals are molecules with unpaired electrons that can react with and damage cellular components due to their reactivity and instability (21, 22). These molecules are typically categorized as reactive oxygen species (ROS) and reactive nitrogen species (RNS) (23). Mitochondria, the powerhouse of the cell, generate ROS as byproducts of oxygen metabolism, including various compounds like hydroxyl radicals, singlet oxygen, peroxides, hypochlorous acid, superoxide, and alpha oxygen (24). RNS, with longer half-lives compared to ROS, consist of peroxynitrite, nitroxyl anion, nitrogen dioxide, nitrosonium cation, and S-nitrosothiols. Numerous enzymes are involved in the formation of free radicals, and the function of these enzymes in generating oxidative stress has been previously reviewed (25).

Indeed, oxidative stress is known as a primary and powerful source of cardiac inflammatory responses caused by secondary injury following MI, playing a crucial role in the development of pathophysiological complications and cell death mechanisms post-MI. Through employing isoproterenol myocardial injury models, it has been established that oxidative stress has a devastating function in the pathophysiology of cardiovascular injury (26). Studies point to the fact that activating MMPs, mitigating tight junction protein expression, implementing changes in the cardiomyocyte structure, and induction of inflammatory signaling pathways are instigated by oxidative stress (27). Also, the role of oxidative stress in

the development of cardioinflammation and cell death by activating Ca^{2+} (28), TGF-β1 (29), and intercellular adhesion molecule-1 (ICAM-1) (30) signaling pathways in MI has been demonstrated. Another study conducted on cardiomyocytes reported that oxidative stress-induced MMP2 expression was attributable to the activation of activator protein 1 and/or nuclear factor kappa B (NF-κB) post I/R injury (31). As a consequence, it confirms that oxidative stress signaling is the principal mechanism underlying cardiovascular impairments associated with MI injury, and inhibiting the formation of oxidative stress has been proposed as a direct approach to developing MI therapy. Despite efforts to treat oxidative damage through exogenous antioxidants or introducing antioxidant genes, clinical trials have not shown significant therapeutic benefits (32, 33). Therefore, addressing oxidative damage-related complications and potentially activating endogenous antioxidant genes via antioxidant peptide therapy presents a promising therapeutic strategy (34).

Overall, oxidative stress emerges as the central driver of secondary injury after MI by promoting inflammation, cardiomyocyte apoptosis, and tissue remodeling. These insights highlight the importance of targeting oxidative stress–related pathways, which provides the rationale for investigating MG53 as a potential therapeutic modulator in MI.

Oxidative Stress and Mitochondrial Damage in MI

Mitochondrial dysfunction resulting from oxidative stress has been extensively studied in the pathogenesis of MI due to its critical role in cellular respiration and various biochemical processes. Oxidative stress can impact mitochondria, which play a key role in the generation of oxidative stress (35). Therefore, oxidative stress-induced mitochondrial dysfunction is a significant focus in understanding the pathogenesis of MI. Oxidative stress affects mitochondria in several ways. It induces mutations in mitochondrial DNA, disrupts the respiratory chain, and disturbs Ca^{2+} homeostasis. Together, these impairments contribute to cellular dysfunction and may lead to tissue degeneration. Oxidative stress primarily targets mitochondrial DNA, inducing mutations and altering its structure and functions (36). Another significant target for oxidative stress is the mitochondrial respiratory chain. The mitochondrial respiratory chain consists of five complexes, namely complexes I, II, III, IV, and V. This series is located in the inner mitochondrial membrane, with the first four complexes constituting the respiratory electron-transport chain. Mitochondrial free radicals are generated at complex I and complex III of the electron transport chain, with complex III being the primary source of mitochondrial ROS generation. Two initial steps identified as direct tissue damage are energy depletion and disruption of Ca^{2+} homeostasis. The impairment of coronary blood flow is a major mechanism of the primary injury in MI (37).

Considering the pathophysiology of MI, mitochondria play a key role in cell death. In MI-induced mechanisms of apoptosis, mitochondrial membrane integrity, Ca^{2+}, and ROS are involved (38, 39). The mitochondrial apoptotic pathways are categorized as caspase-dependent or caspase-independent. The cytochrome complex (Cyt-c) plays a crucial role in caspase-dependent apoptosis, whereas the apoptosis-inducing factor (AIF) is essential in the caspase-independent pathway of apoptosis in MI (40, 41). ROS triggers Bax-dependent mitochondrial outer membrane permeabilization and induces the mitochondrial release of Cyt-c and AIF (42). The efflux of Cyt-c activates caspases, especially caspase-9 and caspase-3, resulting in DNA fragmentation (43).

Another mechanism involved in apoptosis is the dysfunction of the regulation of intracellular Ca^{2+} levels by the endoplasmic reticulum (ER) (44). Studies have shown that calcium exchange between mitochondria and ER, facilitated by the mitochondria-associated ER membrane (MAM), plays a prominent role in MI-induced apoptosis, and caspase-12 is implicated as an important mediator in mitochondria-ER-induced apoptosis (45, 46). Furthermore, in the process of cardiac remodeling following an MI, lysosomal proteases stimulate proteins of the Bcl-2 family. This provocation also indirectly triggers a mitochondrial apoptotic pathway, exemplified by the TNFα/apoptosis signal–regulating kinase 1 (ASK1)/c-Jun N-terminal kinase (JNK) signaling cascade (31) (Figure 1).

In addition to MG53-related mechanisms, several other therapeutic strategies have been explored to directly target mitochondrial dysfunction in MI. Mitochondria-targeted antioxidants, such as mitoquinone mesylate (MitoQ) and visomitin (SKQ1), have shown promise in reducing ROS generation and preserving mitochondrial integrity (47). Pharmacological interventions that stabilize the mitochondrial permeability transition pore (mPTP), including cyclosporine A, have also been investigated to prevent cell death during ischemia-reperfusion (48, 49). Furthermore, enhancing mitophagy and stimulating mitochondrial biogenesis through peroxisome proliferator-activated receptor-γ (PPAR-γ) coactivator-1α (PGC-1α) activators or sirtuin signaling has been suggested as a means to restore mitochondrial homeostasis (50). Metabolic modulators that improve mitochondrial energy efficiency, such as trimetazidine, represent another potential avenue (51). Together, these approaches highlight the therapeutic value of preserving mitochondrial structure and function, and position MG53 within a broader spectrum of cardioprotective strategies.

Recently, there has been significant focus on the development of antioxidant therapies to protect the heart in MI due to advancements in understanding the mechanisms of oxidative stress-induced apoptosis (12, 52, 53). The role and mechanisms of proteins like MG53 in controlling antioxidant genes to alleviate oxidative stress post-MI have been extensively studied. For instance, in 2022, Gamper-Fedos et al. (54) proposed a new mechanism where recombinant human MG53 (rhMG53) treatment could be a promising strategy to reduce cardiac damage and enhance cardiac function in patients post-ischemic injury. Their study demonstrated that rhMG53 treatment

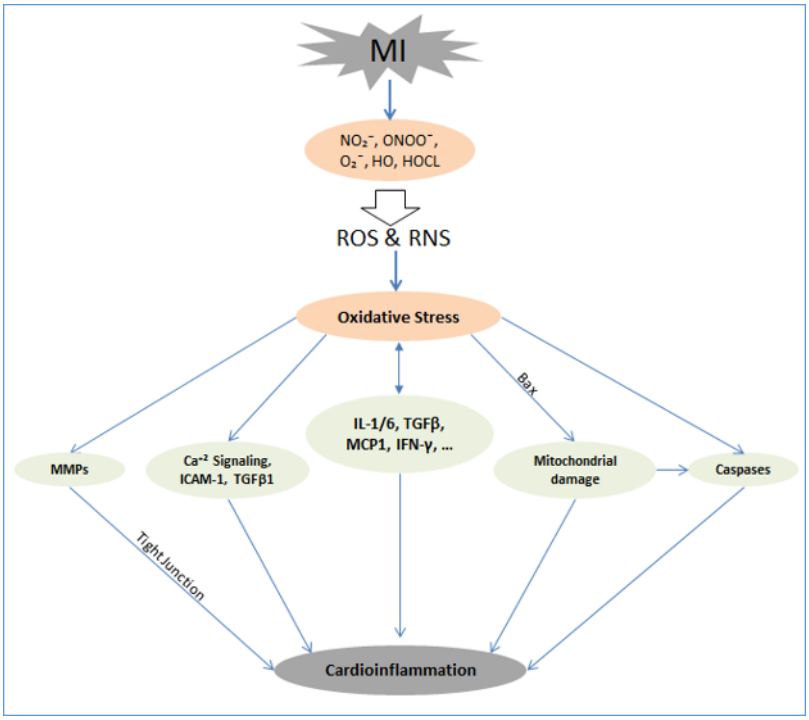

Figure 1. Schematic presentation of oxidative stress-induced in mitochondrial damage and cardioinflammation in myocardial infarction (MI). Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are the primary sources of oxidative stress in MI injury. ROS/RNS activate matrix metalloproteinases (MMPs), transforming growth factor-beta (TGF-β), and other intermediary inflammatory genes, leading to inflammation and cardioinflammation. Additionally, ROS or RNS activate different inflammatory cytokines such as interleukins IL-1β and IL-6 and interferon-gamma (IFN-γ), which contributing to cardioinflammation. Oxidative stress also induces mutations in mitochondrial DNA, impairs the mitochondrial respiratory chain, and disrupts $Ca2^{+}$ homeostasis and defense mechanisms, ultimately causing mitochondrial damage and activating caspases, leading to cardioinflammation. This figure is an original schematic created by the authors.

preserved mitochondrial membrane potential, reduced mitochondrial ROS production, and decreased mitophagy in cardiomyocytes under oxidative stress conditions. However, the study lacked an evaluation of mitochondrial function, which could further clarify the effect of MG53 on preserving mitochondria post-ischemia/reperfusion (I/R) injury. The activation of MG53 as an antioxidant-promoting transcription factor has been shown to mitigate mitochondrial dysfunction and oxidative stress-induced cardiac damage in MI (55). Therefore, understanding the signaling pathways and interactions between MG53 and mitochondria could pave the way for utilizing MG53 as a targeted protein therapy for cardioprotection and other applications in regenerative medicine.

In summary, mitochondria serve both as a major source and a vulnerable target of oxidative stress in MI, leading to apoptosis and impaired cardiac function. Considering the ability of MG53 to preserve mitochondrial integrity, this section underscores why MG53 may represent a promising candidate for mitochondrial-targeted cardioprotection.

Oxidative Stress and Cardiac Remodeling in MI

Structural changes in the heart are inevitable consequences of MI, with left ventricular remodeling being a crucial response to these changes (56, 57). The alterations in the left ventricular wall result from intracellular and extracellular changes in the myocardium (56). Various factors, such as oxidative stress, inflammatory reactions, local ischemia, myocardial cell death, and the production of ROS and inflammatory cytokines, contribute to the biological responses in left ventricular regeneration post-MI (56). All these factors are correlated and result in chronic changes such as left ventricular dilatation with left ventricular dysfunction, which can be referred to as one of the most important factors specifying the prognosis of patients with MI. The degree of left ventricular remodeling can predict mortality and morbidity in patients with MI (56).

Known as pivotal molecules for inducing cell death, ROS directly damage tissue, with their main sources being mitochondria, phagocyte NADPH, and xanthine oxidase (58). As mentioned earlier, ROS and inflammation have a reciprocal relationship, where ROS can stimulate the production of inflammatory cytokines, and vice versa, inflammatory cytokines can stimulate the formation of ROS (59, 60). In the chronic stage, ROS and inflammatory cytokines contribute to the degradation of collagens, the main structural component of cardiomyocytes, leading to left ventricular (LV) dilation, a process facilitated by the activation of MMPs (61). Studies on transgenic mice overexpressing the antioxidant protein SOD have shown a significant reduction in infarction size, highlighting the adverse effects of ROS (62). Additionally, in a study on cardiac hypertrophy, the overexpression of long non-coding RNAs (LncRNAs) controlled cardiac hypertrophy by increasing the expression of transcription factor specificity protein 1 (SP1) through the stimulation of the MG53 signaling pathway (63). Recent research has also demonstrated the role of MG53 in necroptosis, a regulated form of necrotic cell death mediated by receptor-interacting protein kinases (RIPKs). In this process, ROS promotes the

interaction between MG53 and RIPK1 (64, 65).

Therefore, fine-tuning ROS levels in the body could be crucial for treating human ailments. Activating the MG53 signaling pathway may be a potential therapeutic strategy to protect the heart from MI-induced cardiovascular impairments. Future studies should focus on investigating the role of ROS in modulating MG53's function in cardiac preconditioning and post-conditioning.

Collectively, oxidative stress–induced ROS and inflammation drive structural remodeling of the left ventricle, which is closely linked to long-term prognosis after MI. Thus, strategies that activate MG53 and fine-tune ROS levels may help to attenuate maladaptive remodeling and improve cardiac outcomes.

MG53 as a Potential Therapeutic Target for MI

MG53 is a multifunctional protein that, due to its anti-inflammatory and anti-oxidative characteristics, enhances plasma membrane repair and modifies myocardial malfunction caused by various disorders (66, 67). The membrane repair function of MG53 in cardiovascular diseases is accompanied by changes in the oxidative state of the cell. For example, MG53 in ischemic preconditioning (IPC), which is regarded as the most potent intrinsic protector against MI, plays a role. Specifically, a moderate short-term increase of intracellular ROS can trigger MG53 secretion from the heart via H2O2 protein kinase C-delta (PKC-δ) dependent mechanism, and extracellular MG53 can participate in protection against IPC injury. Lack of MG53 increases the damage caused by oxidative stress in IPC conditions (68, 69), as evidenced by the knockdown of MG53 enhancing H2O2-induced cardiomyocyte death. Conversely, the overexpression of MG53 protects cardiomyocytes against oxidative stress-induced cell death (70).

Several preclinical studies have provided direct evidence for the cardioprotective role of MG53 in MI and related conditions. For example, Cao et al. demonstrated that the overexpression of MG53 in mice significantly reduced infarct size and preserved cardiac function after ischemia–reperfusion injury, establishing MG53 as a primary determinant of cardiac ischemic preconditioning (70). Similarly, Shan et al. showed that MG53 secretion is promoted through H2O2-activated PKC-δ signaling during ischemic preconditioning, and knockdown of MG53 aggravated cardiomyocyte death (68). More recently, Gumpper-Fedus et al. have reported that treatment with rhMG53 preserved mitochondrial membrane potential, reduced mitochondrial ROS production, and decreased mitophagy in cardiomyocytes under oxidative stress conditions (54). Beyond MI, systemic administration of rhMG53 has been shown to extend lifespan and attenuate age-related cardiac dysfunction in mice by suppressing NF-κB–mediated inflammation and restoring antioxidant protein expression (71). Collectively, these studies support the therapeutic promise of MG53 and suggest that both protein-based therapy (rhMG53 administration) and gene-modulation strategies hold potential for clinical translation in the treatment of MI.

MG53 plays a central role in ameliorating cytotoxicity and inflammation, which are characteristic features associated with aging, ischemic and chronic diseases caused by increased oxidative stress. MG53 can direct efforts towards exposed phosphatidylserine (PS), a lipid with a negative charge, to facilitate the repair of various damaged tissues. In normal healthy cells, PS is located on the inner leaflet of the plasma membrane. However, when the cell is damaged, PS is distributed to the outer leaflet of the plasma membrane, which serves as a signal for apoptosis detection. In this scenario, cell membrane repair proteins such as Annexins and MG53 converge at the injury site with the assistance of lipid rafts and form a cell membrane repair patch through the stimulation of macrophages (54). In relation to aging, biochemical and histological studies have demonstrated that systemic administration of the rhMG53 protein daily increases the survival of aged mice at the end stage of their life through the reduction of oxidative stress in the condition of myocardial damage. Aging significantly increases the NF-κB mediated inflammatory response and decreases the expression of antioxidant proteins in heart tissue, which were partially recovered by the long-term administration of rhMG53, leading to reduced cardiac inflammation and ROS production (71). After an ROS attack, the protein MG53 binds to cardiolipin. Cardiolipin is a type of phospholipid located on the surface of the inner mitochondrial membrane (72). MG53 then transfers this lipid to the surface of the outer membrane. This function of MG53 helps preserve mitochondrial integrity after oxidative stress by repairing the mitochondrial membrane. This mechanism is similar to the one this protein uses for plasma membrane repair. This process helps reduce the accumulation of mitochondrial ROS and mitigates mitophagy (54). Overall, these events subsequently lead to the upregulation of endogenous scavenging enzymes, including cellular antioxidants such as heme oxygenase 1 (73), catalase, SOD (74, 75), and oxidoreductases like NADPH (76), which have fewer side effects compared to exogenous chemical antioxidants (Figure 2). Also, as a broad-spectrum antioxidant transcription factor, MG53 has the capability to modulate several genes. In vitro studies have shown that MG53 knockout mice are significantly more susceptible to oxidative stress and inflammation compared to wild-type mice (77). Cell-endogenous antioxidants mediate the protective effects of mesenchymal stem cells as well (78). Mesenchymal stem cells play an important role in cardioprotection in conditions of MI through the delivery of CircRNAs, which reduce oxidative stress through an MG53-dependent mechanism and prevent myocardial damage (79). In several other cardiovascular pathophysiological complications, including I/R injury, sepsis-induced myocardial dysfunction, and diabetic cardiomyopathy, dysfunction of MG53 has been associated with oxidative stress. The activation of MG53 is therefore considered a desirable approach to reduce the pathogenesis of these disorders (19).

Recently, the effect of rosuvastatin, an anti-cholesterol

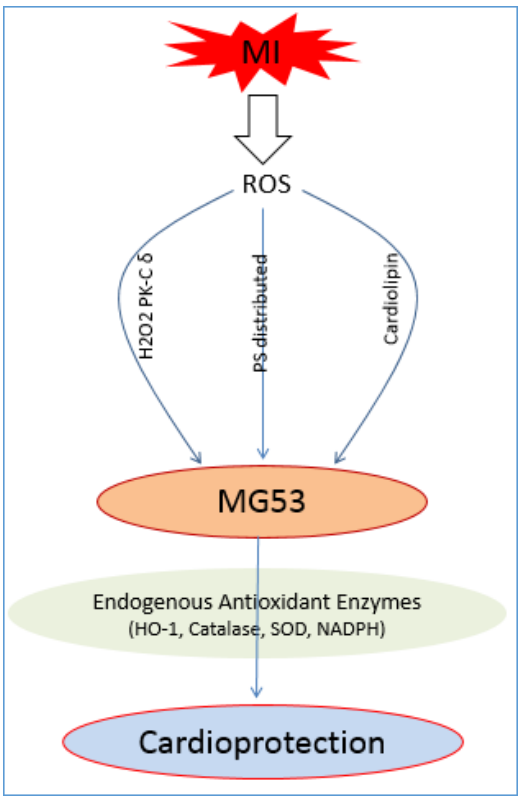

Figure 2. The mechanisms of MG53 activation. Oxidative stress activates MG53 through H2O2 protein kinase C-delta (PKC-δ), phosphatidylserine (PS) distribution, and cardiolipin-dependent mechanisms. Subsequently, activated MG53 triggers the activation of endogenous antioxidant genes such as heme oxygenase 1 (HO-1), catalase, superoxide dismutase (SOD), and nicotinamide adenine dinucleotide phosphate (NADPH), inducing cardioprotection. This figure is an original schematic created by the authors.

compound, in the restoration of cardiomyocytes in myocarditis conditions has been investigated (80). As a cholesterol synthesis inhibitor, rosuvastatin inhibits the NF-κB signaling pathway through an MG53-dependent mechanism and prevents the progression of apoptosis and damage caused by oxidative stress in hyperglycemic conditions (81). These findings could introduce MG53 as a novel potential drug target for myocarditis.

Altogether, preclinical and mechanistic studies consistently support MG53 as a cardioprotective factor with antioxidant, anti-apoptotic, and membrane repair functions. These findings provide a strong foundation for considering MG53-based interventions as future therapeutic approaches for MI.

While current evidence strongly supports the cardioprotective potential of MG53, several questions remain to be addressed in future research. First, more detailed mechanistic studies are required to delineate the molecular interactions of MG53 with mitochondrial and antioxidant signaling pathways. Second, the safety, pharmacokinetics, and optimal delivery methods- rhMG53 or MG53-based gene therapies- must be carefully investigated in preclinical and clinical settings. Third, exploring the role of MG53 in diverse cardiovascular contexts, such as diabetic cardiomyopathy, myocarditis, and heart failure with preserved ejection fraction, may expand its therapeutic scope. Finally, large-scale clinical trials will be necessary to validate the efficacy and long-term outcomes of MG53-based interventions in patients with myocardial infarction. Together, these directions will help translate MG53 research into effective clinical applications.

Discussion

MG53 (TRIM72) has emerged as a multifunctional cardioprotective protein, which has been shown to promote membrane repair, limit oxidative stress, and sustain mitochondrial integrity after myocardial infarction (MI). Studies show consistently that either recombinant human MG53 (rhMG53) or overexpression of MG53 can limit infarct size, decrease apoptosis, and improve cardiac recovery by mechanisms that involve stabilization of mitochondrial membrane potential, inhibition of NF-κB signaling, and upregulation of antioxidant enzymes, such as HO-1 and SOD. Despite these encouraging results, several challenges remain to be solved. Evidence shows that chronic elevation of MG53 might have adverse metabolic effects from the impairment of insulin signaling that is associated with chronic elevation of MG53. In addition, discrepancies with respect to the expression of MG53 in human myocardium raise limits of application of laboratory results to the human situation. In addition, the long-term pharmacokinetics, immunogenicity, and optimal delivery methods of rhMG53 need to be further investigated and clearly defined. Nevertheless, MG53 represents a promising target for therapy. It is the conjunction of membrane repair with mitochondrial and antioxidant protection. More studies are needed to define its relevance in humans, define safe and effective dialoging recommendations, and investigate whether MG53 therapy can be integrated into current reperfusion and cardioprotective studies.

Conclusion

This review highlights the crucial role of oxidative stress in the development and progression of MI, including the activation of inflammatory cytokines, TGF-β, caspases, and cardiomyocyte injury. It also underscores the potential of the MG53 signaling pathway as an antioxidant defense system capable of mitigating these harmful effects. Proper functioning of MG53 is essential for cardiac repair and maintaining homeostasis, yet MI disrupts MG53 secretion and downstream signaling, thereby aggravating oxidative damage. Importantly, MG53 represents a promising therapeutic target for MI. Therapeutically, MG53 can be targeted through strategies such as rhMG53 protein administration, gene therapy approaches to enhance MG53 expression, or small-molecule modulators that activate MG53 signaling pathways. These approaches may strengthen endogenous antioxidant defenses, preserve mitochondrial integrity, and promote cardiomyocyte survival following ischemic injury. Overall, the MG53 signaling pathway provides a novel and attractive direction for the development of targeted therapies against oxidative stress–induced cardiomyopathy in MI. Future studies should further explore the translational potential of

MG53-based therapies and their role in improving clinical outcomes in patients with MI.

Authors' Contribution

Conceptualization: Hossein Azizian.
Data Curation: Zeinab Farhadi.
Formal Analysis: Mansour Esmailidehaj.
Investigation: Hossein Azizian, Zeinab Farhadi, Fatemeh Zare Mehrjardi.
Methodology: Fatemeh Zare Mehrjardi, Mansour Esmailidehaj.
Project Administration: Hossein Azizian.
Resources: Hossein Azizian.
Software: Zeinab Farhadi.
Supervision: Hossein Azizian.
Validation: Hossein Azizian, Mansour Esmailidehaj, Fatemeh Zare Mehrjerdi.
Visualization: Zeinab Farhadi, Fatemeh Zare Mehrjardi.
Writing–Original Draft: Hossein Azizian, Zeinab Farhadi, Mansour Esmailidehaj, Fatemeh Zare Mehrjardi.

Data Availability Statement

All necessary data will available from the corresponding author upon reasonable request.

Funding

This research received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval

Not applicable.

References

1. Tuama RM, Mustafa AA, Yahya ZS. A review on brain-heart axis physiology and its clinical implications. Int J Med Sci 2025;7(1):41-51. doi:https://www.doi.org/10.33545/26648881.2025.v7.i1a.59
2. Campbell E. It's more than the mouth: the effects of periodontal disease on systemic health. Dent Assist 2007;76(3):26-8.
3. World Health Organization (WHO). Cardiovascular Diseases (CVDs): Key Facts. Geneva: WHO; 2021.
4. Ip JH, Levin RI. Myocardial preservation during ischemia and reperfusion. Am Heart J 1988;115(5):1094-104. doi:10.1016/0002-8703(88)90082-8
5. Chapman AR, Shah ASV, Lee KK, Anand A, Francis O, Adamson P, et al. Long-term outcomes in patients with type 2 myocardial infarction and myocardial injury. Circulation 2018;137(12):1236-45. doi:10.1161/circulationaha.117.031806
6. Talman V, Ruskoaho H. Cardiac fibrosis in myocardial infarction-from repair and remodeling to regeneration. Cell Tissue Res 2016;365(3):563-81. doi:10.1007/s00441-016-2431-9
7. Nojiri H, Shimizu T, Funakoshi M, Yamaguchi O, Zhou H, Kawakami S, et al. Oxidative stress causes heart failure with impaired mitochondrial respiration. J Biol Chem 2006;281(44):33789-801. doi:10.1074/jbc.M602118200
8. Duan D, Li H, Chai S, Zhang L, Fan T, Hu Z, et al. The relationship between cardiac oxidative stress, inflammatory cytokine response, cardiac pump function, and prognosis post-myocardial infarction. Sci Rep 2024;14(1):8985. doi:10.1038/s41598-024-59344-5
9. Praetner M, Zuchtriegel G, Holzer M, Uhl B, Schaubächer J, Mittmann L, et al. Plasminogen activator inhibitor-1 promotes neutrophil infiltration and tissue injury on ischemia-reperfusion. Arterioscler Thromb Vasc Biol 2018;38(4):829-42. doi:10.1161/atvbaha.117.309760
10. Neri M, Fineschi V, Di Paolo M, Pomara C, Riezzo I, Turillazzi E, et al. Cardiac oxidative stress and inflammatory cytokines response after myocardial infarction. Curr Vasc Pharmacol 2015;13(1):26-36. doi:10.2174/15701611113119990003
11. Aleksandrowicz M, Konop M, Rybka M, Mazurek Ł, Stradczuk-Mazurek M, Kciuk M, et al. Dysfunction of microcirculation in atherosclerosis: implications of nitric oxide, oxidative stress, and inflammation. Int J Mol Sci 2025;26(13):6467. doi:10.3390/ijms26136467
12. Daiber A, Steven S, Euler G, Schulz R. Vascular and cardiac oxidative stress and inflammation as targets for cardioprotection. Curr Pharm Des 2021;27(18):2112-30. doi:10.2174/1381612827666210125155821
13. Ren Y, Zhang H. Emerging role of exosomes in vascular diseases. Front Cardiovasc Med 2023;10:1090909. doi:10.3389/fcvm.2023.1090909
14. Azizian H, Farhadi Z, Bader M, Alizadeh Ghalenoei J, Ghafari MA, Mahmoodzadeh S. GPER activation attenuates cardiac dysfunction by upregulating the SIRT1/3-AMPK-UCP2 pathway in postmenopausal diabetic rats. PLoS One 2023;18(12):e0293630. doi:10.1371/journal.pone.0293630
15. Ray PD, Huang BW, Tsuji Y. Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling. Cell Signal 2012;24(5):981-90. doi:10.1016/j.cellsig.2012.01.008
16. Rodríguez M, Lucchesi BR, Schaper J. Apoptosis in myocardial infarction. Ann Med 2002;34(6):470-9. doi:10.1080/078538902321012414
17. McElhanon KE, Bhattacharya S. Altered membrane integrity in the progression of muscle diseases. Life Sci 2018;192:166-72. doi:10.1016/j.lfs.2017.11.035
18. Guan F, Huang T, Wang X, Xing Q, Gumpper K, Li P, et al. The TRIM protein mitsugumin 53 enhances survival and therapeutic efficacy of stem cells in murine traumatic brain injury. Stem Cell Res Ther 2019;10(1):352. doi:10.1186/s13287-019-1433-4
19. Ma S, Wang Y, Zhou X, Li Z, Zhang Z, Wang Y, et al. MG53 protects hUC-MSCs against inflammatory damage and synergistically enhances their efficacy in neuroinflammation injured brain through inhibiting NLRP3/caspase-1/IL-1β axis. ACS Chem Neurosci 2020;11(17):2590-601. doi:10.1021/acschemneuro.0c00268
20. Chen J, Wang B, Meng T, Li C, Liu C, Liu Q, et al. Oxidative stress and inflammation in myocardial ischemia-reperfusion injury: protective effects of plant-derived natural active compounds. J Appl Toxicol 2025;45(7):1103-23. doi:10.1002/jat.4719
21. Tian K, Yang Y, Zhou K, Deng N, Tian Z, Wu Z, et al. The role of ROS-induced pyroptosis in CVD. Front Cardiovasc Med 2023;10:1116509. doi:10.3389/fcvm.2023.1116509
22. Poon HF, Calabrese V, Scapagnini G, Butterfield DA. Free radicals and brain aging. Clin Geriatr Med 2004;20(2):329-59. doi:10.1016/j.cger.2004.02.005
23. Zhu H, Itoh K, Yamamoto M, Zweier JL, Li Y. Role of Nrf2 signaling in regulation of antioxidants and phase 2 enzymes in cardiac fibroblasts: protection against reactive oxygen and nitrogen species-induced cell injury. FEBS Lett 2005;579(14):3029-36. doi:10.1016/j.febslet.2005.04.058
24. Dai X, Huang Z, Lyu R. Free radicals in health and disease. MedComm (2020) 2025;6(10) :e70396. doi:10.1002/mco2.70396
25. Andreadou I, Schulz R, Papapetropoulos A, Turan B, Ytrehus K, Ferdinandy P, et al. The role of mitochondrial reactive oxygen species, NO and H2S in ischaemia/reperfusion injury and cardioprotection. J Cell Mol Med 2020;24(12):6510-22. doi:10.1111/jcmm.15279
26. Sundaramoorthy A, Shanmugam N. Potential therapeutic effect of *Salvia coccinea* leaf extract in chronic disorders: myocardial infarction, cataract, and arthritis in rat. Pharm Sci Adv 2023;1(2):100017. doi:10.1016/j.pscia.2023.100017
27. Welcome MO, Dogo D, Nikos EM. Cellular mechanisms

and molecular pathways linking bitter taste receptor signalling to cardiac inflammation, oxidative stress, arrhythmia and contractile dysfunction in heart diseases. Inflammopharmacology 2023;31(1):89-117. doi:10.1007/s10787-022-01086-9
28. Nakamura TY, Nakao S, Wakabayashi S. Neuronal Ca2+ sensor-1 contributes to stress tolerance in cardiomyocytes via activation of mitochondrial detoxification pathways. J Mol Cell Cardiol 2016;99:23-34. doi:10.1016/j.yjmcc.2016.08.013
29. Liang B, Zhang XX, Li R, Zhu YC, Tian XJ, Gu N. Guanxin V alleviates acute myocardial infarction by restraining oxidative stress damage, apoptosis, and fibrosis through the TGF-β1 signalling pathway. Phytomedicine 2022;100:154077. doi:10.1016/j.phymed.2022.154077
30. Singh V, Kaur R, Kumari P, Pasricha C, Singh R. ICAM-1 and VCAM-1: gatekeepers in various inflammatory and cardiovascular disorders. Clin Chim Acta 2023;548:117487. doi:10.1016/j.cca.2023.117487
31. Alfonso-Jaume MA, Bergman MR, Mahimkar R, Cheng S, Jin ZQ, Karliner JS, et al. Cardiac ischemia-reperfusion injury induces matrix metalloproteinase-2 expression through the AP-1 components FosB and JunB. Am J Physiol Heart Circ Physiol 2006;291(4) :H1838-46. doi:10.1152/ajpheart.00026.2006
32. Gardlík R, Pálffy R, Hodosy J, Lukács J, Turna J, Celec P. Vectors and delivery systems in gene therapy. Med Sci Monit 2005;11(4) :RA110-21.
33. Mensah GA, Fuster V, Murray CJL, Roth GA. Global burden of cardiovascular diseases and risks, 1990-2022. J Am Coll Cardiol 2023;82(25):2350-473. doi:10.1016/j.jacc.2023.11.007
34. Mata A, Cadenas S. The antioxidant transcription factor Nrf2 in cardiac ischemia-reperfusion injury. Int J Mol Sci 2021;22(21):111939. doi:10.3390/ijms222111939
35. Xu X, Pang Y, Fan X. Mitochondria in oxidative stress, inflammation and aging: from mechanisms to therapeutic advances. Signal Transduct Target Ther 2025;10(1):190. doi:10.1038/s41392-025-02253-4
36. Suematsu N, Tsutsui H, Wen J, Kang D, Ikeuchi M, Ide T, et al. Oxidative stress mediates tumor necrosis factor-alpha-induced mitochondrial DNA damage and dysfunction in cardiac myocytes. Circulation 2003;107(10):1418-23. doi:10.1161/01.cir.0000055318.09997.1f
37. Xu HX, Cui SM, Zhang YM, Ren J. Mitochondrial Ca2+ regulation in the etiology of heart failure: physiological and pathophysiological implications. Acta Pharmacol Sin 2020;41(10):1301-9. doi:10.1038/s41401-020-0476-5
38. Siasos G, Tsigkou V, Kosmopoulos M, Theodosiadis D, Simantiris S, Tagkou NM, et al. Mitochondria and cardiovascular diseases-from pathophysiology to treatment. Ann Transl Med 2018;6(12):256. doi:10.21037/atm.2018.06.21
39. Gong G, Wan W, Zhang X, Chen X, Yin J. Management of ROS and regulatory cell death in myocardial ischemia-reperfusion injury. Mol Biotechnol 2025;67(5):1765-83. doi:10.1007/s12033-024-01173-y
40. Nan J, Zhu W, Rahman MS, Liu M, Li D, Su S, et al. Molecular regulation of mitochondrial dynamics in cardiac disease. Biochim Biophys Acta Mol Cell Res 2017;1864(7):1260-73. doi:10.1016/j.bbamcr.2017.03.006
41. Vásquez-Trincado C, García-Carvajal I, Pennanen C, Parra V, Hill JA, Rothermel BA, et al. Mitochondrial dynamics, mitophagy and cardiovascular disease. J Physiol 2016;594(3):509-25. doi:10.1113/jp271301
42. Kroemer G, Galluzzi L, Brenner C. Mitochondrial membrane permeabilization in cell death. Physiol Rev 2007;87(1):99-163. doi:10.1152/physrev.00013.2006
43. Li P, Nijhawan D, Budihardjo I, Srinivasula SM, Ahmad M, Alnemri ES, et al. Cytochrome c and dATP-dependent formation of Apaf-1/caspase-9 complex initiates an apoptotic protease cascade. Cell 1997;91(4):479-89. doi:10.1016/s0092-8674(00)80434-1
44. Zhao Q, Hu X, Shao L, Wu G, Du J, Xia J. LipoxinA4 attenuates myocardial ischemia reperfusion injury via a mechanism related to downregulation of GRP-78 and caspase-12 in rats. Heart Vessels 2014;29(5):667-78. doi:10.1007/s00380-013-0418-y
45. Fazal L, Laudette M, Paula-Gomes S, Pons S, Conte C, Tortosa F, et al. Multifunctional mitochondrial Epac1 controls myocardial cell death. Circ Res 2017;120(4):645-57. doi:10.1161/circresaha.116.309859
46. Gao P, Yan Z, Zhu Z. Mitochondria-associated endoplasmic reticulum membranes in cardiovascular diseases. Front Cell Dev Biol 2020;8:604240. doi:10.3389/fcell.2020.604240
47. Kurian GA, Jayaraman S, Gino ER. Strategic targeting of mitochondria: bridging biology and therapy for health benefits. Cell Biochem Biophys 2026;84(1):283-309. doi:10.1007/s12013-025-01915-y
48. Ji Y, Leng Y, Lei S, Qiu Z, Ming H, Zhang Y, et al. The mitochondria-targeted antioxidant MitoQ ameliorates myocardial ischemia-reperfusion injury by enhancing PINK1/Parkin-mediated mitophagy in type 2 diabetic rats. Cell Stress Chaperones 2022;27(4):353-67. doi:10.1007/s12192-022-01273-1
49. Piot C, Croisille P, Staat P, Thibault H, Rioufol G, Mewton N, et al. Effect of cyclosporine on reperfusion injury in acute myocardial infarction. N Engl J Med 2008;359(5):473-81. doi:10.1056/NEJMoa071142
50. Abu Shelbayeh O, Arroum T, Morris S, Busch KB. PGC-1α is a master regulator of mitochondrial lifecycle and ROS stress response. Antioxidants (Basel) 2023;12(5):1075. doi:10.3390/antiox12051075
51. Dézsi CA. Trimetazidine in practice: review of the clinical and experimental evidence. Am J Ther 2016;23(3) :e871-9. doi:10.1097/mjt.0000000000000180
52. Andelova K, Bacova BS, Sykora M, Hlivak P, Barancik M, Tribulova N. Mechanisms underlying antiarrhythmic properties of cardioprotective agents impacting inflammation and oxidative stress. Int J Mol Sci 2022;23(3):1416. doi:10.3390/ijms23031416
53. Rakhshan K, Azizi Y, Naderi N, Ghardashi Afousi A, Aboutaleb N. ELABELA (ELA) peptide exerts cardioprotection against myocardial infarction by targeting oxidative stress and the improvement of heart function. Int J Pept Res Ther 2019;25(2):613-21. doi:10.1007/s10989-018-9707-8
54. Gumpper-Fedus K, Park KH, Ma H, Zhou X, Bian Z, Krishnamurthy K, et al. MG53 preserves mitochondrial integrity of cardiomyocytes during ischemia reperfusion-induced oxidative stress. Redox Biol 2022;54:102357. doi:10.1016/j.redox.2022.102357
55. Xue Y, Song T, Ke J, Lin S, Zhang J, Chen Y, et al. MG53 protects against coxsackievirus B3-induced acute viral myocarditis in mice by inhibiting NLRP3 inflammasome-mediated pyroptosis via the NF-κB signaling pathway. Biochem Pharmacol 2024;223:116173. doi:10.1016/j.bcp.2024.116173
56. Hori M, Nishida K. Oxidative stress and left ventricular remodelling after myocardial infarction. Cardiovasc Res 2009;81(3):457-64. doi:10.1093/cvr/cvn335
57. Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction. Experimental observations and clinical implications. Circulation 1990;81(4):1161-72. doi:10.1161/01.cir.81.4.1161
58. Sies H, Belousov VV, Chandel NS, Davies MJ, Jones DP, Mann GE, et al. Defining roles of specific reactive oxygen species (ROS) in cell biology and physiology. Nat Rev Mol Cell Biol 2022;23(7):499-515. doi:10.1038/s41580-022-00456-z
59. Blaser H, Dostert C, Mak TW, Brenner D. TNF and ROS crosstalk in inflammation. Trends Cell Biol 2016;26(4):249-61. doi:10.1016/j.tcb.2015.12.002
60. Michalak KP, Michalak AZ. Understanding chronic inflammation: couplings between cytokines, ROS, NO, Cai 2+, HIF-1α, Nrf2 and autophagy. Front Immunol 2025;16:1558263.

doi:10.3389/fimmu.2025.1558263
61. Herpel E, Singer S, Flechtenmacher C, Pritsch M, Sack FU, Hagl S, et al. Extracellular matrix proteins and matrix metalloproteinases differ between various right and left ventricular sites in end-stage cardiomyopathies. Virchows Arch 2005;446(4):369-78. doi:10.1007/s00428-004-1177-z
62. Chen Z, Siu B, Ho YS, Vincent R, Chua CC, Hamdy RC, et al. Overexpression of MnSOD protects against myocardial ischemia/reperfusion injury in transgenic mice. J Mol Cell Cardiol 1998;30(11):2281-9. doi:10.1006/jmcc.1998.0789
63. Xu L, Wang H, Jiang F, Sun H, Zhang D. LncRNA AK045171 protects the heart from cardiac hypertrophy by regulating the SP1/MG53 signalling pathway. Aging (Albany NY) 2020;12(4):3126-39. doi:10.18632/aging.102668
64. Wang Q, Park KH, Geng B, Chen P, Yang C, Jiang Q, et al. MG53 inhibits necroptosis through ubiquitination-dependent RIPK1 degradation for cardiac protection following ischemia/reperfusion injury. Front Cardiovasc Med 2022;9:868632. doi:10.3389/fcvm.2022.868632
65. Dabravolski SA, Kalmykov VA, Maksaeva AO, Rozhkova UV, Lapshina KO, Orekhov AN. Necroptosis in myocardial ischaemia-reperfusion injury: current update on mechanisms, therapeutic targets, and translational potential. Apoptosis 2025;30(5-6):1216-34. doi:10.1007/s10495-025-02108-x
66. Su J, Wu S, Zhou F, Tong Z. Research progress of macromolecules in the prevention and treatment of sepsis. Int J Mol Sci 2023;24(16):13017. doi:10.3390/ijms241613017
67. Yun M, Langford L, Russell L, Ndiforamang N, Zhang A, Bai W. Emerging stimuli-responsive hydrogels for enhancing chronic wound healing. RSC Appl Polym 2026;4(1):53-82. doi:10.1039/d5lp00092k
68. Shan D, Guo S, Wu HK, Lv F, Jin L, Zhang M, et al. Cardiac ischemic preconditioning promotes MG53 secretion through H2O2-activated protein kinase C-δ signaling. Circulation 2020;142(11):1077-91. doi:10.1161/circulationaha.119.044998
69. Wang Y, Zhou H, Wu J, Ye S. MG53 alleviates hypoxia/reoxygenation-induced cardiomyocyte injury by succinylation and ubiquitination modification. Clin Exp Hypertens 2023;45(1):2271196. doi:10.1080/10641963.2023.2271196
70. Cao CM, Zhang Y, Weisleder N, Ferrante C, Wang X, Lv F, et al. MG53 constitutes a primary determinant of cardiac ischemic preconditioning. Circulation 2010;121(23):2565-74. doi:10.1161/circulationaha.110.954628
71. Wang X, Li X, Ong H, Tan T, Park KH, Bian Z, et al. MG53 suppresses NF-κB activation to mitigate age-related heart failure. JCI Insight 2021;6(17) :e148375. doi:10.1172/jci.insight.148375
72. Romanova N, Sule K, Issler T, Hebrok D, Persicke M, Thévenod F, et al. Cadmium-cardiolipin disruption of respirasome assembly and redox balance through mitochondrial membrane rigidification. J Lipid Res 2025;66(3):100750. doi:10.1016/j.jlr.2025.100750
73. Zhu XZ, Wang JQ, Wu YH. MG53 ameliorates nerve injury induced neuropathic pain through the regulation of Nrf2/HO-1 signaling in rats. Behav Brain Res 2023;449:114489. doi:10.1016/j.bbr.2023.114489
74. Han X, Chen D, Liufu N, Ji F, Zeng Q, Yao W, et al. MG53 protects against sepsis-induced myocardial dysfunction by upregulating peroxisome proliferator-activated receptor-α. Oxid Med Cell Longev 2020;2020:7413693. doi:10.1155/2020/7413693
75. Zhao L, Cheng J, Liu D, Gong H, Bai D, Sun W. *Potentilla anserina* polysaccharide alleviates cadmium-induced oxidative stress and apoptosis of H9c2 cells by regulating the MG53-mediated RISK pathway. Chin J Nat Med 2023;21(4):279-91. doi:10.1016/s1875-5364(23)60436-4
76. Zhu H, Hou J, Roe JL, Park KH, Tan T, Zheng Y, et al. Amelioration of ischemia-reperfusion-induced muscle injury by the recombinant human MG53 protein. Muscle Nerve 2015;52(5):852-8. doi:10.1002/mus.24619
77. Sermersheim M, Kenney AD, Lin PH, McMichael TM, Cai C, Gumpper K, et al. MG53 suppresses interferon-β and inflammation via regulation of ryanodine receptor-mediated intracellular calcium signaling. Nat Commun 2020;11(1):3624. doi:10.1038/s41467-020-17177-6
78. Esmailidehaj M, Esmaeili H, Chavoushi E, Rezvani ME, Azizian H. Lack of effect of plasma of myocardial preconditioned, ischemic and ischemic-reperfused rats of myocardium on differentiation of mesenchymal stem cells into cardiomyocytes. J Shahid Sadoughi Univ Med Sci 2022;30(4):4778-92. doi:10.18502/ssu.v30i4.9902
79. Li J, Jiang R, Hou Y, Lin A. Mesenchymal stem cells-derived exosomes prevent sepsis-induced myocardial injury by a CircRTN4/miR-497-5p/MG53 pathway. Biochem Biophys Res Commun 2022;618:133-40. doi:10.1016/j.bbrc.2022.05.094
80. Gotto AM Jr. Jeremiah Metzger Lecture: cholesterol, inflammation and atherosclerotic cardiovascular disease: is it all LDL? Trans Am Clin Climatol Assoc 2011;122:256-89.
81. Zhuang J, Cheng G, Huang J, Guo H, Lai Y, Wang J, et al. Rosuvastatin exerts cardioprotective effect in lipopolysaccharide-mediated injury of cardiomyocytes in an MG53-dependent manner. BMC Cardiovasc Disord 2022;22(1):69. doi :https://doi.org/10.1186/s12872-022-02458-3