Sport and Fitness Journal
E-ISSN: 2654-9182 Volume 12, No.1, January 2024: 1-8

EFFECT OF RESISTANCE EXERCISE IN INCREASING ENZYME SUPEROXIDE DISMUTASE AND GLUTATHIONE PEROXIDASE IN SKELETAL MUSCLE: A LITERATURE REVIEW

Liowina Hokky[1*], Ditha Subagiantara[1], Ellisa Koeswanto[1], Indira Juhanna[2], Adiartha Griadhi[2]
[1]Biomedical Anti Aging Medicine Magister Program, Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia.
[2]Department of Physiology, Faculty of Medicine, Universitas Udayana, 80234, Denpasar, Bali, Indonesia.
Email: eugenia.lidwina@yahoo.com

ABSTRACT

Free radicals are produced by skeletal muscles during contraction. Endurance exercise was known to increase the expression of antioxidant enzymes. It is difficult to investigate resistance exercise due to the complex protocol to make the model of resistance exercise. In this review, we would like to concisely explain the effect of resistance exercise in increasing the activity of the antioxidant enzyme. We performed literature searches in several online databases such as PubMed, EMBASE, CENTRAL, and Google Scholar. We performed searching using keywords (resistance exercise) AND (antioxidant enzyme) to find eligible literature. We create a narrative review to discuss the role of resistance exercise in antioxidant enzymes. There were six articles included in this review. There were three articles that reported that resistance exercise increase enzyme glutathione peroxidase. There were five articles that reported an increase in enzyme superoxide dismutase. One article reported no difference in Trx expression after resistance exercise. The duration of exercise was ranging from six to 21 weeks. Duration of 12 weeks was reported in three articles and duration of six, eight, and 21 weeks were reported in one article for each duration. Resistance exercise enhances the expression of the antioxidant enzymes, especially glutathione peroxidase and SOD.

Keywords: glutathione peroxidase; resistance exercise; superoxide dismutase

INTRODUCTION

The discovery of superoxide dismutase (SOD) acts as the root of the advancement of free radical biology research. SOD is found widespread in human tissue which shows the essential function of this enzyme to protect the cell from the damaging effect of superoxide radicals.[1] Besides SOD, there are other enzymes that also act as an antioxidant that plays a role in eliminating free radicals to protect the cells.

The skeletal muscles increase the production of reactive oxygen species (ROS) during contraction.[2] However, the contraction of the skeletal muscle also enhances the expression and activities of several enzymes that eliminate ROS.[3] Exercise like endurance exercise is reported to enhance the activities of several enzymes, such as SOD, glutathione peroxidase, and catalase which act as antioxidants.[4-6] On the other hand, research investigating resistance exercise is limited and inconclusive due to the difficulty of performing a model of resistance exercise. Regarding resistance exercise, there are several research showing the role of resistance exercise in affecting the expression and activity of antioxidant enzymes. In this review, we would like to concisely explain the role of resistance exercise in increasing the expression of these enzymes.

METHODS

This was a narrative literature review study. Eligibility criteria were generated based on the PICO framework. The population was adult males and females; the interest was resistance exercise; the comparator was any comparator; and the outcome was the expression and activity of the antioxidant enzymes following exercise. Based on the PICO framework, the keywords in this review were (resistance exercise) AND (antioxidant enzyme) to perform literature searching. The online

databases were PubMed, EMBASE, CENTRAL, and Google Scholar. We included studies comparing resistance exercise and reported the expression and activity of antioxidant enzymes which were published in English. There was no restriction regarding the year of publication. The findings were narratively elaborated.

The initial literature search using predefined keywords result in 500 articles. After we removed the duplicate articles, we performed title and abstract screening of these 500 articles. There were eight articles that were eligible based on title and abstract screening. However, two articles were excluded due to animal studies. Therefore, we obtained six articles that were eligible for this review.

RESULTS

As can be seen in **Table 1**, we provided a summary of the findings of included articles.

Table 1. Summary of findings of included articles

Author	Sample	Intervention	Result
Brinkmann, *et al*.	Sixteen non-insulin dependent overweight/obese and untrained type 2 diabetic men, who declared to be free of diabetic nephropathy, neuropathy, retinopathy and cardiovascular complications.	Resistance exercise included: leg presses, leg extensions, lat pull-downs, chest presses, abdominal crunches, back extensions, seated rows. .	Resistance exercise twice a week for 3 months did not alter PRDX1, 2, 3, 4, 6 in the skeletal muscle of type 2 diabetes mellitus patients, but significantly increased SOD2 (165.9%), GPX1 (162.4%), PRDX5 (137.5%), and HSP70 (148.5%).
Valls, *et al*.	Twenty-eight volunteers were randomly assigned to either control or trained groups. The average age was 72 ± 1.	12 weeks of explosive-type resistance exercise, two days per week on alternative days. The kind of resistance exercise were leg curl, leg extension, chest press, low row, countermovement jump power, 6 meters walking, 6 meters walking loaded, stair-climbing, stair-climbing loaded	Resistance exercise caused a significant decrease of TrxR1 in the training group (PRE vs. POST: TrxR1/β-actin ratio, 0.61 ± 0.06 vs. 0.28 ± 0.07, $p < 0.05$), while no change of Trx1 and Trx2 expressions ($p > 0.05$).
Garcia-Lopez, *et al*.	Thirty-two healthy middle-aged men. None of them had any background in resistance exercise and not taking any medication known to affect hormonal or metabolic responses to exercise.	The 21-week whole-body resistance exercise was carried out, under supervision, twice a week, with a special emphasis on the lower body. Therefore, each exercise session included two exercises for the leg extensor muscles and one exercise for the leg flexors.	mRNA levels of catalase, glutathione peroxidase (GPx), mitochondrial superoxide dismutase (MnSOD) and cytosolic superoxide dismutase (CuZnSOD) were increased after 21 weeks of resistance exercise.
Mesquita, *et al*.	Thirteen males aged 64 ± 9 years.	Full-body resistance exercise twice a week for 6 weeks. Each session was composed of leg press, leg extensions, leg curls, barbell bench press, cable pulldowns.	Resistance exercise significantly increased the mRNA expression of all assayed antioxidants (SOD1: $p = 0.018$, 95% CI (0.22, 1.82); SOD2: $p = 0.027$, 95% CI (0.10, 1.28); CAT: $p = 0.032$, 95% CI (0.07, 1.13); GPx-1: $p = 0.022$, 95% CI (0.10, 1.59)) except for GSR, which presented a trend to increase but did not reach

			statistical significance (p = 0.092, 95% CI (−0.11, 1.12)).
Parise, *et al*.	Twelve men with the average age of 71.2 ± 6.5 years, with an average weight of 88.8 ± 11.3 kg, an average height of 147.7 ± 4.8 cm, and an average body fat of 21.4 ± 3.6%.	Resistance exercise was performed three times weekly on non-consecutive days for 12 weeks. Resistance exercise for each session consisted of 3 sets of 10 repetitions each of unilateral leg press and leg extension.	Resistance exercise resulted in a significant increase in CuZnSOD (pre—7.2 ± 4.2, post—12.6 ± 5.6; p = 0.02) and catalase (pre—8.2 ± 2.3, post—14.9 ± 7.6; p = 0.02) but not MnSOD activity.
Azizbeigi, *et al*.	Thirty untrained males with no experience of formal physical activity volunteered to participate in this study and were assigned to one of three homogeneous groups: resistance (n = 10), endurance (n = 10), and concurrent (n = 10).	The resistance exercise protocol was performed with progressive loading three times/week on nonconsecutive days for 8 weeks, and included circuit training. The movements included were chest press, lateral pull down, leg extension and flexion, biceps and triceps curl, squat, and sit-ups (with 90- and 180-second intervals between sets and cycles, respectively).	SOD significantly increased by 9.54% (p = 0.032). The MDA level significantly decreased by 32% in the resistance group (p = 0.025)

DISCUSSION

The contracting skeletal muscle is known to enhance the production of ROS in the skeletal muscle itself.[2,7] The primary free radicals that are increased after the skeletal muscle contraction are nitric oxide (NO) and $O_2^{\bullet-}$.[4,8] The NO production by skeletal muscle is facilitated by nitric oxide synthases.[9] Furthermore, the production of $O_2^{\bullet-}$ is facilitated by xanthine oxidase (XO), phospholipase A2 (PLA2), and nicotinamide adenine dinucleotide oxidases (NOX).[10,11]

The source of ROS after the skeletal muscle contraction is not from the mitochondrial rather it is associated with NOX with the transverse tubules and plasma membrane.[10-12] In skeletal muscle, there are two isoforms of NOX which are NOX2 and NOX4. The location of NOX2 is specifically in the sarcolemma, while the location of NOX4 is in the mitochondria and reticulum sarcoplasm.[13] The ROS production during skeletal muscle contraction is mainly mediated by NOX2.[10,12]

Besides NOX, PLA2 also has a role in increasing the production of ROS in contracting skeletal muscle following exercise.[14,15] XO is also reported to enhance ROS production during the contraction of skeletal muscle. Actually, the location of XO expression is not in the skeletal muscle fibers but within the capillary endothelial cells which surround the muscle fibers. The contraction of the skeletal muscle itself causes activation of XO and produces $O_2^{\bullet-}$ radicals surrounding the muscle fiber.[16,17] In capillary endothelial cells, NOX4 also increases ROS production during skeletal muscle contraction.[18] The $O_2^{\bullet-}$ radicals are transformed into H_2O_2 by SOD in the extracellular and are able to cross the sarcolemma and cause a prooxidative reaction in muscle fibers.[19]

The antioxidant is a molecule that prevents or lowers the oxidation rate of the substrate.[4] There are two layers of antioxidants which are small non-enzymatic molecules and antioxidants enzyme. The small non-enzymatic molecules are including glutathione and uric acid as non-dietary antioxidants and vitamins E and C as dietary antioxidants. However, dietary antioxidants are unable to effectively overcome the reaction rate of oxidation.[20] Therefore, the additional defense to prevent oxidative damage is antioxidant enzymes.[21] The location of key cellular antioxidant enzymes is in various compartments of the cell to remove the oxidants in various locations.[19]

The source of all ROS in cells is eventually the $O_2^{\bullet-}$ radical. Actually, the $O_2^{\bullet-}$ radicals are not super reactive but these molecules can be transformed into highly reactive radicals including H_2O_2

and peroxynitrite. The H_2O_2 could diffuse over a long distance and produce high reactive species and causing oxidation. Therefore, to protect the cells from oxidation, the removal of $O_2^{\bullet-}$ radical and H_2O_2 is essential.[19]

SOD is the enzyme to facilitate the dismutation and transforms the $O_2^{\bullet-}$ radicals into hydrogen peroxide.[1] SOD enzyme is further divided into three isoforms and all of them require transition metal to activate the enzyme activity in the active site.[22] SOD1 and SOD2 are located intracellularly while SOD3 is in the extracellular space. Furthermore, the location of SOD1 in intracellular is specifically in the cytosol and mitochondrial intermembrane space. Meanwhile, the location of SOD2 in the intracellular is specifically only in the mitochondrial matrix. SOD1 needs copper and zinc to activate the enzymatic activity, while SOD2 needs manganese as a cofactor.[23] SOD 3 requires similar transition metal as SOD 1 as a cofactor, which includes copper and zinc.[24,25]

Enzyme glutathione peroxidase is divided into eight isoforms. All of the isoforms require the transition metal of selenium to activate the enzymatic activity. The GPX uses reducing equivalents of glutathione to transform H_2O_2 and organic hydroperoxides into H_2O or alcohol.[4,26,27] The location of each isoform is different and compartmentalized so this enzyme can reduce the peroxides in multiple locations.[19] The location of GPX1 is specifically in the muscle cell's cytosol and mitochondria. The location of GPX2 is in the cytosol of muscle cells, only while the location of GPX3 is specifically in the cytosol of muscle cells and extracellular space.[26] Further, the location of GPX4 is only in mitochondria and specifically works to reduce lipid peroxide.[28]

Enzyme catalase plays a role in the reduction of H_2O_2 into water and oxygen.[29] Catalase needs iron as a cofactor but does not require reducing equivalents similar to GPX to remove H_2O_2. Catalase is unable to reduce organic hydroperoxides. Catalase is located in several compartments of cells which include peroxisomes, cytosol, and mitochondria.[30]

Peroxiredoxins (PRDXs) an enzyme that removes peroxides in the cells.[31] PRDX does not require transition metal as a cofactor to activate the enzyme activity. Rather, this enzyme uses cysteine residues for the catalysis process.[32,33] The expression of PRDXs is high in the cells. Therefore, most of the peroxide in the cytosol (99%) and mitochondria (90%) are reduced by this enzyme.[32] So it can be concluded that the removal of peroxides in the cells is facilitated by catalase, GPX, and PRDX where PRDX is the dominant one.[19]

There are six isoforms of PRDX, which include PRDX1 to PRDX6. They use electrons that are provided by thioredoxin to reduce H_2O_2, alkyl peroxides, and peroxynitrite. The PRDXs are located in the mitochondria, cytosol, peroxisomes, and nucleus to reduce H_2O_2, alkyl peroxides, and peroxynitrite in various compartments of the cell.[33]

Thioredoxin (Trx) is a low-molecular-weight antioxidant protein that is expressed in all cell types. This protein cause reduction of many target enzyme including PRDXs.[34] Thioredoxins system consists of two components which include Trx and Trx reductase (TrxR). TrxR is further divided into TrxR1, TrxR2, and TrxR3. The location of TrxR1 is in the cytosol and the location of TrxR2 is specifically in the mitochondria.[34] The location of TrxR3 is exclusively in the testes.[35] The function Trx is transferring electrons to the enzyme which leads to the reduction of cellular enzymes. Then, the TrxR reduces the oxidized form of Trx using electrons from NADPH and makes Trx a redox modulator.[34]

Trx also has function as an antioxidant. It is done by transferring electrons to methionine sulfoxide reductase and acts as protein disulfide reductase. The Trx activity as protein disulfide reductase is essential in the process of regenerating the oxidized proteins. Trx also has a role in targeting the antioxidant gene expression through the regulation of transcription factors activity including P53, AP-1, and nuclear factor kappa B (NF-kB).[3]

During resistance exercise, free radicals are produced through the pathway of xanthine oxidase, neutrophil burst, autooxidation of catecholamine, ischemia of muscle cells, and transformation of weak superoxide into strong hydroxyl radicals which mediates by lactate. The strong hydroxyl radicals cause oxidative stress.[36,37]

The electron donation to oxygen leads to the formation of reactive oxygen (superoxide) anions in the mitochondria. SOD cause dismutation which transforms the superoxide radicals into H_2O_2. The enzyme glutathione peroxidase and catalase could transform the H_2O_2 to H_2O. On the other hand, the Fenton reaction can alternatively cause the formation of OH radicals from the hydrogen

peroxide. The superoxides and OH radicals cause the proteins and lipids oxidation in the cell which further leads to cell damage.[38]

Even can cause cellular damage, ROS also has a function in the regulation of signaling for growth, differentiation, proliferation, and apoptosis of the cell. During exercise, mitochondrial biogenesis is an important process to saturate energy depletion. ROS also regulates transcriptional coactivators such as PGC-1α which is required for mitochondrial biogenesis.[38]

In skeletal muscle, ROS activates the nuclear factor kappa-light-chain-enhancer of activated B (NF-κB) and p38 MAPK which leads to the activation of PGC-1α when phosphorylated. Furthermore, ROS also has a function in the regulation of Ca^{2+} signaling where Ca^{2+} signaling has an autoregulation function of PGC-1α via MEF2.[39-41] There is a network between PGC-1α and ROS, where ROS regulates PGC-1α production, and PGC-1α regulates ROS production.[42-46] As has been described, the production of ROS in skeletal muscle is increased during exercise. On the other hand, the production of PGC-1α is also increased and PGC-1α could activate antioxidant enzymes to reduce the ROS.[38]

The expression of enzyme GPx1 and SOD2 in skeletal muscle is increased along with the increased expression of PGC-1α. These antioxidant enzymes removed the superoxide and hydrogen peroxide.[44-46] The PGC-1α has a function in regulating the antioxidant enzyme, especially in the glutathione system and MnSOD.[47] On the other hand, antioxidants also can affect PGC-1α expression. It is shown by increasing the PGC-1α expression following the glutathione depletion after the exercise through p53.[48]

Endurance exercise is known to increase the expression cellular antioxidant defense system.[49] However, there are only a few articles investigating the effect of resistance exercise on the expression of cellular antioxidant enzymes.[50-52] It is because of the difficulty to performed resistance exercise protocol in the animal model. The resistance exercise in rats model is reported to enhance the expression and activity of antioxidant enzymes such as SOD, SOD1, and total GPX in skeletal muscles.[50,52] However, resistance exercise has no role in increasing the activity of catalase in skeletal muscle.[50,52] Furthermore, resistance exercise increases the activity of the antioxidant enzyme in skeletal muscle in type II diabetes mellitus, middle-aged men, and older adults.[53-57] Resistance exercise also increases the mRNA levels and the activity of catalase, GPX, SOD1, and SOD2 in skeletal muscle in humans.[53,55-57] Resistance exercise increases the activities of PRDX5, glutathione reductase, and TrxR1 in skeletal muscle.[53,54,56]

Azizbeigi *et al*. reported that SOD increase by 9.54% from the baseline following resistance exercise. The MDA level was also significantly decreased by 32% following resistance exercise.[58] Garcia-Lopez *et al*. also reported upregulation of mRNA levels of the catalase, GPX, and SOD in middle-aged men following 21 weeks of resistance exercise.[55] The training intensity did not affect the protective effect of resistance exercise to oxidative stress because different training intensities led to similar decreases in MDA levels and increases in glutathione.[59] Besides that, resistance exercise also increases the total antioxidant capacity.[60] In the elderly, Parise *et al*. reported that a resistance exercise program within 12 weeks increases the activity of SOD and catalase.[57]

The limitation of this review is we were unable to describe specific resistance exercises to increase antioxidant enzymes because we did not find any article describing this. Therefore, future studies should investigate which specific resistance that provides the most for enhancing the antioxidant enzyme.

CONCLUSION

Resistance exercise ranging from six to 21 weeks increases the expression of antioxidant enzymes following exercise. However, the specific resistance exercise which increases the antioxidant enzyme is still inconclusive. The PGC-1α plays an important role in increasing the expression of SOD and glutathione system antioxidants following resistance exercise.

CONFLICT OF INTEREST

There is no conflict of interest related to the materials or methods used in this study.

FUNDING

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

AUTHOR CONTRIBUTION

The authors took part in the manuscript, contribute to data collection, and participated in writing the manuscript and all agree to accept equal responsibility for the accuracy of the content of this article.

REFERENCES

1. Zhao H, Zhang R, Yan X, Fan K. Superoxide dismutase nanozymes: An emerging star for anti-oxidation. *J Mater Chem B*. 2021; 9(35): 6939 – 6957.
2. Powers SK, Schrager M. Redox signaling regulates skeletal muscle remodeling in response to exercise and prolonged inactivity. *Redox Biol*. 2022; 54: 102374.
3. Morrison D, Hughes J, Gatta PAD, Mason S, Lamon S, Russell AP, Wadley GD. Vitamin C and E supplementation prevents some of the cellular adaptations to endurance-training in humans. *Free Radic Biol Med*. 2015; 89: 852 – 62.
4. Powers SK, Deminice R, Ozdemir M, Yoshihara T, Bomkamp MP, Hyatt H. Exercise-induced oxidative stress: Friend or foe? *J Sport Health Sci*. 2020; 9(5): 415 – 425.
5. Wang P, Li CG, Qi Z, Cui D, Ding S. Acute exercise stress promotes Ref1/Nrf2 signalling and increase mitochondrial antioxidant activity in skeletal muscle. *Exp Physiol*. 2016; 101(3): 410 – 20.
6. Di Meo S, Napolitano G, Venditti P. Mediators of physical activity protection against ROS-linked skeletal muscle damage. *Int J Mol Sci.* 2019; 20: 3024.
7. Powers SK, Radak Z, Ji LL. Exercise-induced oxidative stress: Past, present and future. *J Physiol.* 2016; 594: 5081 – 5092.
8. Jackson MJ. Redox regulation of muscle adaptations to contractile activity and aging. *J Appl Physiol (1985)*. 2015; 119(3): 163 – 71.
9. Balke JE, Zhang L, Percival JM. Neuronal nitric oxide synthase (nNOS) splice variant function: Insights into nitric oxide signaling from skeletal muscle. *Nitric Oxide*. 2019; 82: 35 – 47.
10. Jackson MJ, Vasilaki A, McArdle A. Cellular mechanisms underlying oxidative stress in human exercise. *Free Radic Biol Med.* 2016; 98: 13 – 17.
11. Sakellariou GK, Jackson MJ, Vasilaki A. Redefining the major contributors to superoxide production in contracting skeletal muscle. The role of NAD(P)H oxidases. *Free Radic Res.* 2014; 48: 12 – 29.
12. Sakellariou GK, Vasilaki A, Palomero J, Kayani A, Zibrik L, McArdle A, Jackson MJ. Studies of mitochondrial and nonmitochondrial sources implicate nicotinamide adenine dinucleotide phosphate oxidase(s) in the increased skeletal muscle superoxide generation that occurs during contractile activity. *Antioxid Redox Signal.* 2013; 18: 603 – 621.
13. Ferreira LF, Laitano O. Regulation of NADPH oxidases in skeletal muscle. *Free Radic Biol Med.* 2016; 98: 18 – 28.
14. Lee K-P, Shin YJ, Cho SC, Lee SM, Bahn YJ, Kim JY, *et al*. Peroxiredoxin 3 has a crucial role in the contractile function of skeletal muscle by regulating mitochondrial homeostatis. *Free Radic Biol Med.* 2014; 77: 198 – 306.
15. Pal R, Basu Thakur P, Li S, Minard C, Rodney GG. Real-time imaging of NADPH oxidase activity in living cells using a novel fluorescent protein reporter. *PLoS ONE*. 2013; 8: e63989.
16. Wadley GD, Nicolas MA, Hiam DS, McConell GK. Xanthine oxidase inhibition attenuates skeletal muscle signaling following acute exercise but does not impair mitochondrial adaptations to endurance training. *Am J Physiol Endocrinol Metab*. 2013; 304(8): E853 – 62.
17. Sagor MAT, Tabassum N, Potol MA, Alam MA. Xanthine oxidase inhibitor, allopurinol, prevented oxidative stress, fibrosis, and myocardial damage in isoproterenol induced aged rats. *Oxid Med Cell Longev*. 2015; 2015: 478039.
18. Vogel J, Kruse C, Zhang M, Schroder K. Nox4 supports proper capillary growth in exercise and retina neo-vascularization. *J Physiol*. 2015; 593: 2145 – 2154.
19. Powers SK, Goldstein E, Schrager M, Ji LL. Exercise training and skeletal muscle antioxidant enzyme: An update. *Antioxidants (Basel)*. 2022; 12(1): 39.
20. Forman HJ, Davies KJ, Ursini F. How do nutritional antioxidants really work: Nucleophilic tone and para-hormesis versus free radical scavenging in vivo. *Free Radic Biol Med*. 2014; 66: 24 – 35.
21. Lei XG, Zhu JH, Cheng WH, Bao Y, Ho YS, Reddi AR, Holmgren A, Arner ES. Paradoxical roles of antioxidant enzymes: Basic mechanisms and health implications. *Physiol Rev*. 2016; 96: 307 – 364.

22. Fetherolf MM, Boyd SD, Taylor AB, Kim HJ, Wohlschlegel JA, Blackburn NJ, *et al*. Copper-zinc superoxide dismutase is activated through a sulfenic acid intermediate at a copper ion entry site. *J Biol Chem*. 2017; 292(29): 12025 – 12040.
23. Yan Z, Spaulding HR. Extracellular superoxide dismutase, a molecular transducer of health benefits of exercise. *Redox Biol*. 2020; 32: 101508.
24. Lewandowski L, Kepinska M, Milnerowicz H. The copper-zinc superoxide dismutase activity in selected diseases. *Eur J Clin Investig.* 2019; 49: e13036.
25. Lewandowski L, Kepinska M, Milnerowicz H. Alterations in concentration/activity of superoxide dismutases in context of obesity and selected single nucleotide polymorphism in genes: SOD1, SOD2, SOD3. *Int J Mol Sci*. 2020; 21(14): 5069.
26. Brigelius-Flohe R, Flohe L. Regulatory phenomena in the glutathione peroxidase superfamily. *Antioxid Redox Signal.* 2020; 33: 498 – 516.
27. Powers SK, Deminice R, Ozdemir M, Yoshihara T, Bomkamp MP, Hyatt H. Exercise-induced oxidative stress: Friend or foe? *J Sport Health Sci.* 2020; 9: 415 – 425.
28. Seibt TM, Proneth B, Conrad M. Role of GPX4 in ferroptosis and its pharmacological implication. *Free Radic Biol Med.* 2019; 133: 144 – 152.
29. Glorieux C, Calderon PB. Catalase, a remarkable enzyme: Targeting the oldest antioxidant enzyme to find a new cancer treatment approach. *Biol Chem.* 2017; 398: 1095 – 1108.
30. Halliwell BAJG. *Free Radicals in Biology and Medicine.* Oxford; London, UK: 2015.
31. Lu J, Holmgren A. The thioredoxin antioxidant system. *Free Radic Biol Med*. 2014; 66: 75 – 87.
32. Karplus PA. A primer on peroxiredoxin biochemistry. *Free Radic Biol Med.* 2015; 80: 183 – 190.
33. Rhee SG, Kil IS. Multiple functions and regulation of mammalian peroxiredoxins. *Annu Rev Biochem.* 2017; 86: 749 – 775.
34. Balsera M, Buchanan BB. Evolution of the thioredoxin system as a step enabling adaptation to oxidative stress. *Free Radic Biol Med.* 2019; 140: 28 – 35.
35. Zhang J, Duan D, Osama A, Fang J. Natural molecules targeting thioredoxin system and their therapeutic potential. *Antioxid Redox Signal.* 2021; 34: 1083 – 1107.
36. Papoti M, da Silva ASR, Araujo GG, Santiago V, Martins LEB, Cunha SA, Gobatto CA. Aerobic and anaerobic performances in tethered swimming. *Int J Sports Med.* 2013; 34(8): 712 – 9.
37. Peake JM, Neubauer O, Gatta PAD, Nosaka K. Muscle damage and inflammation during recovery from exercise. *J Appl Physiol*. 2017; 122(3): 559 – 570.
38. Thirupathi A, de Souza CT. Multi-regulatory network of ROS: The interconnection of ROS, PGC-1 alpha, and AMPK-SIRT1 during exercise. *J Physiol Biochem*. 2017; 73(4): 487 – 494.
39. Theeuwes WF, Gosker HR, Schols AMWJ, Langen RCJ, Remels AHV. Regulation of PGC-1α expression by GSK-3β-TFEB signaling axis in skeletal muscle. *Biochim Biophys Acta Mol Cell Res*. 2020; 1867(2): 118610.
40. Goldstein I, Paakinaho V, Baek S, Sung M-H, Hager GL. Synergistic gene expression during the acute phase response is characterized by transcription factor assisted loading. *Nat Commun.* 2017; 8(1): 1849.
41. Kain V, Kapadia B, Viswakarma N, Seshadri S, Prajapati B, Jena PK, *et al*. Co-activator binding protein PIMT mediates TNF-α induced insulin resistance in skeletal muscle via the transcriptional down-regulation of MEF2A and GLUT4. *Sci Rep*. 2015; 5: 15197.
42. Baldelli S, Aquilano K, Ciriolo MR. PGC-1α buffers ROS- mediated removal of mitochondria during myogenesis. *Cell Death Dis*. 2014; 6: e1515.
43. Fu X, Yao K, Du X, Li Y, Yang X,Yu M, *et al.* PGC- 1α regulates the cell cycle through ATP and ROS in CH1 cells. *J Zhejiang Univ Sci B*. 2016; 17(2): 136 – 146.
44. Ballmann C, Tang Y, Bush Z, Rowe GC. Adult expression of PGC-1α and -1β in skeletal muscle is not required for endurance exercise-induced enhancement of exercise capacity. *Am J Physiol Endocrinol Metab*. 2016; 311(6): E928 – E938.
45. Sun L, Zang W-J, Wang H, Zhao M, Yu X-J, He X, *et al*. Acetylcholine promotes ROS detoxification against hypoxia/reoxygenation-induced oxidative stress through FoxO3a/PGC-1α dependent superoxide dismutase. *Cell Physiol Biochem*. 2014; 34(5): 1614 – 25.
46. Garcia-Quintans N, Prieto I, Sanchez-Ramos C, Luque A, Arza E, Olmos Y, Monsalve M. Regulation of endothelial dynamics by PGC-1α relies on ROS control of VEGF-A signaling. *Free Radic Biol Med.* 2016; 93: 41 – 51.
47. Karkoulias G, McCrink KA, Maning J, Pollard CM, Desimine VL, Patsouras N, *et al*. Sustained GRK2-dependent CREB activation is essential for α_2-adrenergic receptor-induced PC12 neuronal differentiation. 2020; 66: 109446.
48. Aquilano K, Baldelli S, Pagliei B, Cannata SM, Rotilio G, Ciriolo MR. p53 orchestrates the PGC-1alpha-mediated antioxidant response upon mild redox and metabolic imbalance. *Antioxid Redox Signal*. 2013; 18: 386 – 399.

49. Gomez-Cabrera M-C, Salvador-Pascual A, Cabo H, Ferrando B, Vina J. Redox modulation of mitochondriogenesis in exercise. Does antioxidant supplementation blunt the benefits of exercise training? *Free Radic Biol Med.* 2015; 86: 37 – 46.
50. Gomes MJ, Pagan LU, Lima ARR, Reyes DRA, Martinez PF, Damatto FC, *et al*. Effects of aerobic and resistance exercise on cardiac remodelling and skeletal muscle oxidative stress of infarcted rats. *J Cell Mol Med.* 2020; 24: 5352 – 5362.
51. Murlasits Z, Lee Y, Powers SK. Short-term exercise does not increase ER stress protein expression in cardiac muscle. *Med Sci Sports Exerc.* 2007; 39: 1522 – 1528.
52. Scheffer DL, Silva LA, Tromm CB, da Rosa GL, Silveira PC, de Souza CT, *et al*. Impact of different resistance training protocols on muscular oxidative stress parameters. *Appl Physiol Nutr Metab.* 2012; 37: 1239 – 1246.
53. Brinkmann C, Chung N, Schmidt U, Kreutz T, Lenzen E, Schiffer T, *et al*. Training alters the skeletal muscle antioxidative capacity in non-insulin-dependent type 2 diabetic men. *Scand J Med Sci Sports.* 2012; 22: 462 – 470.
54. Beltran Valls MR, Dimauro I, Brunelli A, Tranchita E, Ciminelli E, Caserotti P, *et al*. Explosive type of moderate-resistance training induces functional, cardiovascular, and molecular adaptations in the elderly. *Age.* 2014; 36: 759 – 772.
55. Garcia-Lopez D, Hakkinen K, Cuevas MJ, Lima E, Kauhanen A, Mattila M, *et al*. Effects of strength and endurance training on antioxidant enzyme gene expression and activity in middle-aged men. *Scand J Med Sci Sports.* 2007; 17: 595 – 604.
56. Mesquita PHC, Lamb DA, Godwin JS, Osburn SC, Ruple BA, Moore JH, *et al*. Effects of resistance training on the redox status of skeletal muscle in older adults. *Antioxidants.* 2021; 10: 350.
57. Parise G, Phillips SM, Kaczor JJ, Tarnopolsky MA. Antioxidant enzyme activity is up-regulated after unilateral resistance exercise training in older adults. *Free Radic Biol Med.* 2005; 39: 289 – 295.
58. Azizbeigi K, Stannard S, Atashak S,, Mosalman Haghighi M. Antioxidant enzymes and oxidative stress adaptation to exercise training: Comparison of endurance, resistance, and concurrent training in untrained males. *J Exercise Sci Fitness*. 2014; 12(1): 1 – 6.
59. Ceci R, Valls MRB, Duranti G, Dimauro I, Quaranta F, Pittaluga M, *et al*. Oxidative stress responses to a graded maximal exercise test in older adults following explosive-type resistance training. *Redox Biol*. 2014; 2: 65 – 72.
60. Park S-Y, Kwak Y-S. Impact of aerobic and anaerobic exercise training on oxidative stress and antioxidant defense in athletes. *J Exercise Rehab*. 2016; 12(2): 113 – 117.