

The function and mechanism of SOD in human healthHuajie Zhu¹, Zlachevsky Vicky², Yucui Zhu³¹Corresponding author E-mail: jacksun689@gmail.com. Department of Pathology, Columbia University, New York, Jacksun Easy Biotech, New York, USA. The 2nd Affiliated Hospital of Zhengzhou University;²University of Düsseldorf, Cologne, Heinrich Heine, Germany;³Department of Medicine, Columbia University, New York, USA

Abstract: In human history, many diseases in human life affect the health and longevity of human beings through some unknown factors. Since the separation of superoxide dismutase from bovine red blood cells for the first time in 1938, McCord et al. rediscovered this protein in 1969 and officially named it as superoxide dismutase (EC1.15.1.1, SOD). That is, after the advent of SOD, many questions about human health and longevity have been answered, which has greatly improved human health and longevity. The key to its improvement is to understand that free radical is an important pathogenic factor in the process of human life, and SOD free radical scavenger is the patron saint of maintaining health and prolonging life. In this paper, the pathogenesis of free radicals and how SOD scavenges free radicals are summarized and described.

[**The function and mechanism of SOD in human health**]. *Biomedicine and Nursing* 2019; 5(1): 115-118]. ISSN 2379-8211 (print); ISSN 2379-8203 (online). <http://www.nbmedicine.org>. 12. doi:10.7537/marsbnj050119.12.

Keywords: SOD, superoxide dismutase, Anti-aging, free radicals, antioxidant, Health, longevity, Tumors, heart disease, atherosclerosis, reperfusion injury,

1. Introduction:

As we all know, open the history of each country in the world, look at the history of each country in the life of the emperors, there is a common characteristic, once ruled a country, are looking for the discovery of talent, smart, intelligent experts and scholars, to help the emperor to find immortal elixir. In fact, it is not only the emperor who seeks immortality. But years and generations have passed, and no one has discovered that there is any medicine or measure to make people immortal. Until 1938, was first isolated from bovine erythrocyte Superoxide Dismutase (SOD), and to rediscover the protein, such as 1969 McCord found their biological activity, and make clear its catalytic properties of ultra-oxygen anion disproportionation reaction, formally named Superoxide Dismutase (SOD

, EC1.15.1.1) makes the human study forever a leap in the history of life science. The discovery of SOD makes it possible for human beings to hope to live forever. Regardless of whether or not can achieve immortality, however, the discovery of SOD, prolong the life of human is possible, the important factor is the scientific research has proved that human disease and aging, happens with Free radicals (Free radical) is associated with increased in the body, and SOD is a natural Free radical scavenger, Free radicals are cleared, or the amount of Free radicals in the body, can decrease the occurrence of diseases, This is why the discovery of SOD is a major breakthrough and revolution in the study of human immortality. SOD scavenges the free radicals that cause diseases, which will certainly make the human body healthy and prolong life. This paper aims to comprehensively

expound the role and mechanism of SOD in human health.

2. What is SOD?

Superoxide dismutase (SOD) is the only active enzyme recognized by the international scientific community that can eliminate the harmful free radicals produced in the process of human metabolism. It has the special effect of anti - aging to human body. Superoxide Dismutase (SOD, EC1.15.1.1, SOD) has been studied for more than 70 years since it was first isolated from bovine red blood cells in 1938. In 1969, McCord et al. rediscovered this protein, and discovered their biological activity, and figured out the nature of its catalytic superoxide anion dismutation reaction, so they officially named it as superoxide dismutase

3. What are free radicals?

3.1. What are Free radical? Free radicals, also known as "free groups" in chemistry, refer to atoms or groups with unpaired electrons formed by homolysis of covalent bonds of molecules of compounds under external conditions such as light and heat. The fragments formed have an unpaired electron, such as H·, CH· and Cl·, which are called free radicals

3.2. Free radical writing, generally adding a "·" next to the atomic symbol or atomic group symbol to indicate that there are no pairs of electrons. For example, hydrogen radical (H·, namely hydrogen atom), chlorine radical (Cl·, namely chlorine atom), methyl radical (CH·);

3.3. Age and history: the first known and confirmed free radical was the triphenyl radical discovered by

Moses Grunberg at the University of Michigan in 1900. Chinese organic chemist Youcheng Liu is an academician in the field of free radical chemistry, also made outstanding contributions.

4. How free radicals act on the human body to cause diseases:

Because free radicals contain unpaired electrons, they are extremely unstable (especially hydroxyl radicals), and therefore take electrons from neighboring molecules (including fats, proteins, and DNA) to keep themselves in a stable state. In this way, the neighboring molecule becomes a new free radical, and then grabs the electron....As a result of this chain reaction, the structure of the cell is destroyed, resulting in loss of cell function, gene mutation, and further development into different diseases.

5. Sources of common free radicals:

5.1. Automatic oxidation, some molecules in the body, such as catecholamine, hemoglobin, myoglobin, cytochrome C and mercapto in the process of oxidation will produce free radicals;

5.2. Enzymatic oxidation, some oxidative processes catalyzed by enzymes produce free radicals; **5.1.** In the environment of 12 minutes, the enzyme life has almost no loss, and the enzyme is more than 90 percent.

5.3. When breathing in, phagocytes produce free radicals when scavenging foreign microorganisms.

5.4. Drugs, such as certain antibiotics, anticancer drugs produce free radicals in the body, especially at high oxygen levels.

5.5. Radiation, electromagnetic radiation and particle radiation produce free radicals in the body;

5.6. Smokes the grass, smokes the meeting to produce the massive free radical;

5.7. Non-organic particles, inhaled asbestos, quartz or silica dust, phagocytes in the lungs to produce free radicals;

5.8. Gases, ozone produces free radicals;

5.9. Other things that happen, as you might expect, include fever, heavy use of steroids, or hyperthyroidism, which increases the metabolic rate in the body and produces more free radicals. Industrial gases, pesticides, anesthetic gases and organic solvents in the air outside the body also produce free radicals in the body

6. Possible mechanism of free radical harm to human body:

6.1. Weaken the resistance of cells and make the body susceptible to bacterial and bacterial infections;

6.2. Produce cell-damaging chemicals and form carcinogenic substances;

6.3. It hinders the normal development of cells, interferes with their recovery function, and makes the cell renewal rate lower than the wilt rate;

6.4. Destroy the genetic gene (DNA) tissues in the body, disrupt the operation and regeneration function of cells, cause gene mutation and evolve into cancer;

6.5. Damage the mitochondria (energy stores) in cells, causing oxidative fatigue;

6.6. Destroy the cell membrane, interfere with the cell metabolism, and make the cell membrane lose its function of protecting cells;

6.7. The invasion of amino acids necessary for cell tissues and hormones interferes with the operation of the system in the body, leading to a vicious cycle and more free radicals. The chain reaction can lead to free radical damage throughout the body;

6.8. Damage proteins and enzymes in the body, leading to inflammation and aging;

6.9. Destroy adipose, make lipid peroxidation, bring about atherosclerosis, and produce disease of heart head blood-vessel;

6.10. Destroy carbohydrates, degrade hyaluronic acid, and lead to arthritis, etc.

7. Free radicals and human disease:

7.1. Role of SOD in free radical and tumor formation;

Free radicals have a strong oxidative ability to cause irreversible damage to cell DNA, and some damage to DNA is the basis for the occurrence of malignant tumors. Therefore, the formation of malignant tumors is indeed related to the increase of free radicals. In the process of free radical and tumorigenesis, which is a relatively long process, if the content of SOD in the body is increased and the scavenging effect of free radical is increased, the tumorigenesis may be reduced.

7.1.1. Carcinogenic substances must be metabolized and converted into free radicals by physical and chemical factors before they are likely to cause cancer; Therefore, it suggests that how to induce the generation of free radical substances may lead to the occurrence of tumors;

7.1.2. There is a considerable time dynamic parallel between the ability to generate free radicals and the ability to cause cancer;

7.1.3. When the body's ability to resist free radicals (SOD) is strong, no tumor will occur;

7.1.4. Tumor occurs when the body's ability to resist free radicals (SOD) is weak;

7.1.5. Liu benxian, shen wenmei et al. reported that SOD activity in almost all cancer patients was often lower than normal. Therefore, SOD supplementation can prevent the occurrence of tumor.

7.2. The role of SOD free radicals in the occurrence of senescence;

Aging is a complex phenomenon in which the physiological functions of various organs gradually decrease and decline with age. Aging involves many internal and external factors. Harman pointed out that the accumulation of free radicals may be the root cause of aging. However, aging is a relatively long process. If the content of SOD in the body is increased and the scavenging effect of free radicals is increased, the occurrence and development of aging may be delayed. The main mechanism of free radical promoting aging is related to metabolic disorders in the following aspects.

7.2.1. Freely induced lipofuscin formation:

Excessive oxidation of unsaturated fatty acids in cell membrane by $\cdot O$ and $\cdot OH$ leads to lipid peroxidation, cross-linking and polymerization into lipofuscin (an inert waste that is difficult to eliminate), which accumulates in cells to poison cells and prevent the transmission of intracellular substances and information. Lipofuscin accumulates in skin cells and forms senile plaques. In the accumulation of brain cells, it will cause memory loss or mental disorders, and even lead to senile dementia; It accumulates in the heart muscle cells and the heart loses its function. Collagen aggregation causes skin to lose tension and elasticity, wrinkles, and age-related bone hyperplasia. These are the basic characteristics of aging.

7.2.2. Free induction of mitochondrial DNA mutations:

Human mitochondrial DNA (mtDNA) is a circular double stranded super helix DNA, which exists in the mitochondrial matrix. MtDNA has an extremely economical genetic arrangement, no introns, but some regional genes are reused, so any mutation may cause pathological changes in important functions. Mutations in the mtDNA of germ line cells can cause defects in inherited oxidative phosphorylation (OXPHOS), leading to premature degenerative disease. MtDNA fragment deletion or point mutation can lead to aging, myocardial ischemia, senile heart failure and other senile heart diseases. Loss of fragment in aged myocardium and decreased activity of enzyme in OXPHOS can lead to accelerated free radical mediated lipid peroxidation and the formation of atherosclerotic plaques.

7.2.3. Freely induced apoptosis:

The senescent death of cell is apoptosis. Free radicals in the body, especially the O_2 and $\cdot OH$, mainly produced in the has important function, high activity, high oxygen consumption of body tissues such as brain cells, nerve cells, myocardial and endocrine cells, and cause excessive accumulation,

they attacked through oxidation life macromolecular substances, lead to the organization of DNA in the cell, protein, lipid membrane damage. Induce cell apoptosis and accelerate the aging process.

7.2.4. Free-induced fatigue and SOD anti-fatigue:

Excessive free radicals remain in the body, just as toxins accumulate in the body, making people easily tired, tired, unfocused, often lethargic, and yawning. It has been reported that SOD has a significant effect on the fatigue caused by office workers staying up late working overtime and students coping with exams. It can improve their spirits and concentration, and contribute to the improvement of work performance and examination results.

7.2.5. Free radical-induced reduction in protein synthesis:

Free radicals by its strong oxidation of nucleic acid oxidation and crosslinking, and make a break, mutation, thus seriously affect the normal transcription and translation of protein genetic information, lower the amount of protein expression and even disappear, or produce mutant protein, and protein synthesis to reduce is age-related memory loss, mental retardation, and muscle atrophy.

7.2.6. Comprehensive research conclusions;

The aging process involves many internal and external factors. Harman pointed out that the toxic effects of free radical aggregation and the gradual damage to bone tissue and organs throughout the body may be the root cause of aging.

7.3. The mechanism of SOD free radical and atherosclerosis and reperfusion injury of heart, cerebral thrombosis - heart and brain;

Cardiac and cerebral ischemia is caused by atherosclerosis and abnormal performance of blood pressure caused by a variety of factors, thus leading to cardiac and cerebral thrombosis. The ischemic process before and after thrombosis, and the root cause of reperfusion injury after thrombus removal are from the role of free radicals.

7.3.1. The combination of free radicals and low-density lipoprotein is an important mechanism of atherosclerosis;

Oxidized free oxygen group combines with LDL to form oxidized low density lipoprotein (ox-Ld.). The oxidized low density lipoprotein will be regarded as a foreign body in the blood vessel wall and will be gobbled up by macrophages, monocytes, endothelial cells and smooth muscle cells. Smooth muscle cells and macrophages to consume a large amount of type oxidized low density lipoprotein, its itself become foam cells, a large amount of foam cell accumulation, protrude the blood vessel walls (angiography is to see but do not bleeding wall there are any changes), the formation of atherosclerotic plaques leads to the

occurrence of atherosclerosis of the important mechanisms.

7.3.2. Cerebral ischemia increases free radicals:

During cerebral ischemia, ATP is not utilized and degraded into hypoxanthine successively. Meanwhile, calcium ions activate protease to convert xanthine dehydrogenase into xanthine oxidase, which makes a large amount of accumulated hypoxanthine produce superoxide anions.

7.3.3. Accumulation of free radicals in hypoxemia;

Ischemia before and after thrombus has already affected the metabolism of tissues. During hypoxemia, enzyme free radicals accumulate, and superoxide anion and oxidase are generated by self-oxidation during reperfusion.

7.3.4. Reperfusion increases free radical production:

The ferrous sulfate complex oxidizes itself to produce superoxide anions. After reperfusion, the cycle of tricarboxylic acid has not been restored, but the perfusion provides glucose needed for glycolysis, thus aggravating acidosis and damage to the body.

8. How SOD scavenges free radicals and is beneficial to health;

8.1. SOD scavenging free radical antioxidant chain system

With the further research on SOD, it is found that SOD has formed a complete antioxidant chain in vivo. Superoxide dismutase (SOD), glutathione peroxidase (gsp-px), catalase (CAT) and peroxidase (POD) constitute a complete antioxidant chain system, which can help remove excess free radicals in the body at any time. In addition, there are other substances involved in the direct scavenging of free radicals, such as some antioxidants such as vitamin C, vitamin E, reduced glutathione, carotene and selenium;

8.2. Mechanism of SOD on free radical scavenging:

SOD and glutathione peroxidase are free radical scavenging enzymes that produce toxic H₂O₂ while scavenging free radicals. However, catalase (CAT) and peroxidase (POD) are two auxiliary enzymes for free radical scavenging. When the toxic H₂O₂ increases, CAT and POD, two enzyme auxiliary enzymes, decompose H₂O₂ into pollution-free H₂O and O₂. It catalyzes the reaction of: 2·O + 2·OH + H₂O₂ + O₂. •O is called a superoxide anion radical.

9. Correlation between SOD content and health, free radical medical experiment confirmed;

9.1. Before the age of 25 healthy body SOD content and free radicals in the blood is the basic balance, SOD in normal human serum: enzyme rate method (37 °C) : serum specific activity (activity) : 242 ~ 620 u/L

9.2. After the age of 25, SOD produced by the human body itself cannot remove more and more free radicals, and excess free radicals begin to gradually damage the body;

9.3. At the age of 40, SOD content was only half;

9.4. By the age of 60, the content of SOD is only one fourth, and the free radicals in the body are constantly produced. The function of SOD in scavenging free radicals is out of balance, which leads to the disorder of immune regulation mechanism of the body and the damage of cells and tissues in multiple parts of the body, and finally leads to the occurrence of diseases.

10. Conclusion;

Free radical is an important electron transport carrier in the metabolic process of human body. SOD is a natural free radical scavenging system in the body. Due to different environmental factors, the increase of free radicals and the decrease of SOD are important factors for the occurrence of diseases and aging. The study on the amount and amount of SOD and free radicals in the body is very important to ensure that human beings can reduce the occurrence of diseases and prolong aging, how to reduce the production of free radicals in the body, and how to increase the content of free radicals in the body.

References:

1. Verma S, Alam R, Ahmad I, Singla D, Ali K, Hussain ME. Effect of glycemic control and disease duration on cardiac autonomic function and oxidative stress in type 2 diabetes mellitus. *J Diabetes Metab Disord.* 2018 Sep 8; 17(2):149-158.
2. Huber W: Orgotein--(bovine Cu-Zn superoxide dismutase), an anti-inflammatory protein drug: discovery, toxicology and pharmacology. *European Journal of Rheumatology and Inflammation*, 1981; 4(2):173-182.
3. O.M. Ighodaroab O.A. Akinloyeb: First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid, *Alexandria Journal of Medicine*, 2018:54(4):287-293.
4. S Moncada E A Higgs: The discovery of nitric oxide and its role in vascular biology, *British Journal of Pharmacology*, 2006: 147 :(S1):S193-S201.
5. Vincent Nivière Email author Marc Font cave: Discovery of superoxide reductase: an historical perspective, *JBIC Journal of Biological Inorganic Chemistry*, 2004:9(2):119-123.
6. Joe M. McCorda Marvin A. Edeasb: SOD, oxidative stress and human pathologies: a brief history and a future vision, *Biomedicine & Pharmacotherapy*, 2005, 59(4):139-142.

7. Giuseppe L. Squadron William A. Pryor: The formation of peroxynitrite in vivo from nitric oxide and superoxide, *Chemico-Biological Interactions*, 1995;96(2):203-206.
Volume 96, Issue 2, 19 May 1995, Pages 203-206
8. Edwin Hoa Keyvan Karimi Galougahiab Chia-Chi Liua Ravi Bhindiab Gemma A. Figtreeab, *Biological markers of oxidative stress: Applications to cardiovascular research and practice*, *Redox Biology*, 2013;1(1):483-491.
9. Igor N Zelko, Thomas J Mariani†Rodney J Folz: Superoxide dismutase multigene family: a comparison of the CuZn-SOD (SOD1), Mn-SOD (SOD2), and EC-SOD (SOD3) gene structures, evolution, and expression, *Free Radical Biology and Medicine*, 2002;33(3):3370349.
10. Lu Miao Daret K.St. Clair: Regulation of superoxide dismutase genes: Implications in disease, *Free Radical Biology and Medicine*, 2009;47(4):334-356.
11. Munehiro Kitada, Shinji Kume, Noriko Imaizumi and Daisuke Koya: Resveratrol Improves Oxidative Stress and Protects Against Diabetic Nephropathy through Normalization of Mn-SOD Dysfunction in AMPK/SIRT1-Independent Pathway, *Diabetes* 2011; 60(2): 634-643.
12. Tomasz J. Guzikm, David G. Harrison: Vascular NADPH oxidases as drug targets for novel antioxidant strategies, *Drug Discovery Today*, Volume 11, Issues 11–12, June 2006:11(11-12):524-533.
13. Gidon CzapskiSara Goldstein: Superoxide Scavengers and SOD or SOD Mimics, *Antioxidants in Therapy and Preventive Medicine: The properties and structures of Glutathione Cu (II) complexes and SOD activity*, *Inorganic Chemical Act*, 1983: 79:261-262.
14. Mauro C. Dal Cantoa Mark E. Gurneyb: Neuropathological changes in two lines of mice carrying a transgene for mutant human Cu, Zn SOD, and in mice overexpressing wild type human SOD: a model of familial amyotrophic lateral sclerosis (FALS), *Brain Research*, 1995:676(1):25-40.
15. Rita Bettino, A.N. Balamurugan12, Suzanne Bertera, Massimo Pietropaolo, Massimo Trucco and Jon D. Piganelli: Preservation of Human Islet Cell Functional Mass by Anti-Oxidative Action of a Novel SOD Mimic Compound, *Diabetes* 2002; 51(8): 2561-2567.
16. Gldon Czapski & Sara Goldstein: The Uniqueness of Superoxide Dismutase (SOD) — Why Cannot Most Copper Compounds Substitute Sod In vivo? , Your search for Author: Czapski, Gldon, 1988:4(4):225-229.
17. Albert A. RizvanovMarat A. Mukhamedyarov András PalotásEmail authorRustem R. Islamov: Retrogradely transported siRNA silences human mutant SOD1 in spinal cord motor neurons, *Experimental Brain Research*, 2009:195(1):1-4.
18. F.T. Unger, B. Rabe, A. Harasym, K. Pursche, C. Rosenbrock, H. Juhl, K.A. David: 851 Top Down LC-MALDI Discovery of Cu/Zn SOD as Potential Biomarker for Intrinsic Chemoresistance, *European Journal of Cancer*, 2012:48(5):204-205.
19. Joe M.Mc Cord Irwin Fridovich: Superoxide dismutase: The first twenty years (1968–1988), *Free Radical Biology and Medicine*, 1988:5(5-6):363-369.
- /

3/16/2019