

## SOD and Free Radical Discovery with the Research Status and Future in Human Health

Huaijie Zhu<sup>1</sup>, Zlachevsky Vicky<sup>2</sup>, Yucui Zhu<sup>3</sup>

<sup>1</sup>Corresponding author E-mail: [jacksun689@gmail.com](mailto:jacksun689@gmail.com). Department of Pathology, Columbia University, New York, Jacksun Easy Biotech, New York, USA. The 2<sup>nd</sup> Affiliated Hospital of Zhengzhou University;

<sup>2</sup> University of Düsseldorf, Cologne, Heinrich Heine, Germany;

<sup>3</sup>Department of Medicine, Columbia University, New York, USA

**Abstract:** In the 1830s, Mann and Keilin isolated a blue copper-based protein from bovine red blood cells and liver, and named this protein as **blood copper protein**. As the precursor of the discovery of SOD, they began to confirm the discovery and naming of SOD in the 1970s. With the process of discovery, the scavenging function of SOD on free radicals was gradually realized. With the development of the research on the scavenging function of SOD on free radicals, medical and biological scientists have come up with a new concept and discovery on the occurrence and understanding of aging and anti-aging in human health; 1) to recognize and find the REDOX signal, the understanding and establishment of the concept of oxidative antioxidant and anti-aging, which is a new understanding of the occurrence and development of human aging in medical science; 2) it is found that inflammation is also a concept of oxidative stress, which enables people to establish new therapeutic theories and concepts for many diseases related to inflammation; 3) understanding and discovery of the concept of physiological function of superoxide anions, recognizing that immune cells use free radicals to kill bacteria, the concept of free radical balance has been gradually confirmed. The above three aspects are the previously unknown concepts and understandings established in the discovery and research of SOD, laying a new research approach for the occurrence and development of many unknown diseases, the discovery of possible causes for many diseases with unknown causes makes it possible to find effective treatment schemes without thinking of treatment. SOD may be used as an enzyme for the treatment and prevention of many diseases.

[SOD and Free Radical Discovery with the Research Status and Future in Human Health]. *Biomedicine and Nursing* 2018; 4(4): 97-100]. ISSN 2379-8211 (print); ISSN 2379-8203 (online). <http://www.nbmedicine.org>. 12. doi:[10.7537/marsbnj040418.12](https://doi.org/10.7537/marsbnj040418.12).

**Keywords:** SOD, superoxide dismutase, Anti-aging, free radicals, antioxidant1, Health, longevity.

### 1. Introduction:

The discovery of SOD enables the biomedical industry to have a more comprehensive understanding and understanding of health, aging and anti-aging, especially the role of free radicals in the process of health and aging, but also a series of new understanding. Since the discovery of free radicals around 1900, many studies have focused on the disadvantages of free radicals to organisms, never considering the advantages of free radicals to organisms. With the discovery of SOD and the in-depth research on SOD scavenging free radicals, it is gradually realized that the oxidation and REDOX signals in the organism and the dynamic balance of free radicals in the body are important metabolic processes in the health, aging and anti-aging of organisms. It is possible to achieve aging, anti-aging and healthy longevity in human life only when we master the oxidation and REDOX signals in the organism and the dynamic balance of free radicals in the body. The further study of SOD and free radical discovery in human health will make it possible for human health and anti-aging.

### 2. The initial discovery and understanding of SOD and free radical:

In the 1830s, Mann and Keilin separated a blue copper protein from bovine red blood cells and liver and named it blood copper protein, which was the earliest discovery of SOD (superoxide dismutase) and was considered as a single protein at that time. Mann and Keilin went on to discover similar proteins containing iron and manganese ions, but it was not clear what they were doing. The first free radical ever discovered and confirmed was the triphenyl radical discovered by Moses gunberg at the university of Michigan in 1900, The free radical dimerizes in isolation from air to form “hexaphenylethane .”

Simple organic radicals, such as methyl and ethyl radicals, were confirmed in the 1920s by gas phase reactions. Free radical was also discovered by Linus Pauling in the 1930s during the research on radiation-treated water. The yield of superoxide anions is dependent on the concentration of oxygen in water. Later, the pKa of superoxide anionic conjugate acid was determined by the radiochemist with pulse ray technology, and the kinetic properties

of superoxide anion self-dismuting reaction were studied. Later, the pKa of superoxide anionic conjugate acid was determined by the radiochemist with pulse ray technology, and the kinetic properties of superoxide anion self-dismuting reaction were studied to determine the absorption spectrum of this substance.

### 3. SOD discovery and naming:

Two scientists, Irwin Fridovich and his student JoeMcCord, first gave an oral presentation at a meeting of the federation of American societies for experimental biology, then published it in the form of an analytical technique in the journal JBC in 1969. Tracing its discovery process; Irwin Fridovich and his student JoeMcCord optimized the purification method of this protein and determined that the blood copper protein has the activity of superoxide anion dismutase, and named this kind of protein SOD according to this function. According to Fridovich, the discovery was made in 1968, an eventful year that began with the spring offensive in Vietnam, the assassination in April of Dr. Martin Luther King jr. a prominent black American activist, and the assassination in June of representative Robert f. Kennedy. In Dr Martin Luther King was assassinated on the same day, April 4, duke university campus to a simple enzyme kinetics experiment two scientists Joe m. McCord and IrwinFridovich discovered a new enzyme, according to the active named superoxide dismutase (SOD), its unique role is to clear a super oxygen anion oxygen derived free radicals. Although the technology benefited from the study of radiochemistry, the physical chemists who began to study superoxide anions did not accept the existence of superoxide anions in biological systems and enzymes that catalyzed the dismutation of the substance.

As more and more evidence proved the validity of this finding, it was finally widely accepted. With this discovery, more types of SOD were discovered soon after by gel electrophoresis analysis. SOD soon became a star molecule, and all the international conferences on metalloproteinases and REDOX enzymes were important centers and must-have topics. With the discovery of SOD, more and more scientists have devoted themselves to SOD research. In the first five years, the research on SOD has been divided into two major topics, one is the research on the chemistry and enzymology of SOD protein, the other is the research on the source and chemical activity of superoxide anions in biological systems. Since then, SOD and free radicals began to function and value in the biological system.

studied to determine the absorption spectrum of this

### 4. SOD function identification:

Since April 4, 1968, duke university scientists Joe m. McCord and IrwinFridovich have discovered superoxide dismutase (SOD), a superoxide anion radical derived from oxygen, after many researches, scientists all over the world recognized that SOD is a kind of active protease containing metal elements and named as superoxide dismutase (SOD). At present, the worldwide biomedical industry is developing SOD through different channels. The ministry of health of China has approved SOD as one of the substances with anti-aging, immune regulation, blood lipid regulation, anti-radiation and cosmetic functions, and the legal number is ecl.15.1.1.CAS [905489] 1. Meanwhile, the role of superoxide dismutase has been recognized in the world as follows:

US patent no. (CN1152337A): for the prevention and treatment of local cerebral hemorrhage, ulcers, inflammation, arrhythmia, edema, poisoning, rheumatism, rheumatoid arthritis, and radiation damage, drug poisoning and other diseases. Peng huang, Ph.D., of the University of Texas at Houston's Anderson cancer center, and his colleagues found that superoxide dismutase (SOD) selectively kills leukemia cells without damaging normal tissue cells.

France registered patent no. : (CN1167441A): for the prevention and treatment of specific brain injury, non-specific brain injury caused by brain dysfunction.

European patent number (499621): for the prevention and treatment of cancer and brain damage caused by postoperative radiotherapy and chemotherapy, as well as the inhibition of the re-formation or spread of cancer cells.

Japan patent number (4327541 4312533): for the treatment of organ transplantation after the immune response has a magic effect. A drug used to treat localized bleeding in the brain that leads to nerve necrosis and to prevent hemiplegia.

In Taipei hospital, superoxide dismutase (SOD) was used to treat burn and scald.

### 5. SOD scavenging function of free radicals laid the foundation for the discovery and understanding of new concepts in human health:

#### 5.1. Understanding and establishment of REDOX signal, oxidative antioxidant and anti-aging concepts:

With the discovery of SOD and the further study of its function, the research on human aging and anti-aging is promoted. On the one hand, for the first time to determine the free radicals and the health of the body, the correlation between aging and anti-aging

and close contact, on the other hand, the free radical biology research out of expensive instrument can be successfully applied to adjuvant therapy after radiation therapy, control the progress of heart disease and the treatment of severe arthritis. In Denmark, people are treated with sod for arthritis.

SOD is used as a supplement to food, and it is possible to maintain a high level of sod in the human body, which is to provide the appropriate nutrition for the liver to synthesize sods while consuming the food, or directly to the external source sod in the food protein, which is not digested by the digestive system, and into other parts of the body

SOD development in the field of medical application depends on the further study of its mechanism and the generation mechanism, and is expected to find the catalyst for sod. Because of the different sources of sod, the detection methods vary, and the activity of sod is not known. We expect the standard of international passing to be normalized by science, simplicity and practical principles. Because animal blood sod is blocked in the European Union, the development of plants and microbes sod is a promising industrial direction.

A type of superoxide disintegrase is a major project of the country "15" 863 plan (topic number: : 2004aa214080,2007aa100604), which is developed by the national key laboratory of China university institute, which has been developed by the new generation of sod.

The new generation of sod enzyme products have the following characteristics:

1. The extraction of biological fermentation, the risk of non-haematous disease and cross-infection;
2. In the environment of 12 minutes, the enzyme life has almost no loss, and the enzyme is more than 90 percent.
3. The stability of the system is high, and the enzyme is stable in the pH4.00 range of 11.0, and the enzyme is maintained at room temperature for two years, and the sod enzyme is unique in the world.

#### **6. the academic value and future of SOD:**

In June 1976, the first sod superoxide diversity symposium in the United States was held in the United States, and in the 5th international sod academic conference in 1989, the famous American biochemist, professor Michelson, was consistent with the scientific and applied research of sod, which not only had significant theoretical and practical significance, but also had significant economic value and broad application outlook.

China's sod research, which began in the late 1970s and 1980s, has set off a wave of sod research, and in 1988, it was held in ningbo in 1990, and lanzhou held two national academic seminars.

Shanghai, shantou, etc., and then hold too many sod workshops.

The development of sod in China in the early 21st century has been in a downturn for nearly a decade, and the national sod industry alliance in 2010 marks a new milestone in the sod industry, and again the east sod research is hot. In 2010, the sod was used in the national case of the national example, the key research topic of the science and research institute, and was promoted by the science knowledge education special film of the cctv4 film, and the popularization of the knowledge of sod science and health. The first sod of China's first sod, the first sod of China's chief professor of student engineering, was born, and in the past two years, the sixth national sod academic seminar was held, the national sod production application seminar and the sod high academic conference marketing conference, which is the representative of the enterprise. The national scientists and the professional researchers were lured by the huge magnet, and they were again involved in the study of sod, which was on a straight line and was not able to clean up.

The international comprehensive biomedical information bibliography database, currently the most authoritative biomedical literature database medline network, has included more than 30, 000 sod papers in May 2010, which is only a paper for medicinal purposes. In the first decade of 1989, the paper has more than 2,000 sod papers. It is not hard to see that the interest of sod in 30 years has increased.

Biomedical studies have shown that sod has a wide range of applications, one of which is important because of its potential medicinal value. Sod, a medicinal enzyme, has not yet been able to carry the pharmacopoea, but has been widely used in the United States and Europe, with orgogotein, ormetein, hm-1 ontosein, paloseinorn and so on, the royal pharmaceutical society's publishing of the "2" and "the" 3 "collections. The Chinese muscle injection pig red blood cell sod has been reviewed (the second type of new drug) of the Chinese country, but the existing research is only a small piece of the sea of the medicinal potential, although there is still a difficulty in the research road, but the scientists are still working on the possibilities of extracting the clinical application of sod.

According to the study of sod, the study of sod and free radicals, especially sod and free radicals, will be valuable and discovered before the existence of human health and longevity.

#### **References:**

1. 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.

2. 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.
3. 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.
4. Lu Miao Daret K.St. Clair: Regulation of superoxide dismutase genes: Implications in disease, *Free Radical Biology and Medicine*, 2009:47(4):334-356.
5. Vincent Nivière Email author Marc Fontecave: Discovery of superoxide reductase: an historical perspective, *JBIC Journal of Biological Inorganic Chemistry*, 2004:9(2):119-123.
6. 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.
7. Giuseppe L. Squadrito 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. 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.
10. 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.
11. 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.
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*, *Inorganica Chimica Acta*, 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 Bottino, 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. 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.
17. Albert A. RizvanovMarat A. Mukhamedyarov Andrés 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. JingkeGuoaYueChenbBinYuanbShutaoLiuaPingf anRaoa: Effects of Intracellular Superoxide Removal at Acupoints with TAT-SOD on Obesity: *Free Radical Biology and Medicine*, 2011:51(12)2185-2189.

12/19/2018