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SOD B® & Cell Aging Prevention

Aging is one of the most important socio-sanitary problems in western countries and characterized by a progressive decline in biological functions with time. Cell damages induced by Reactive Oxygen Species (ROS) are a major determinant of life span. ROS levels are increased with age in major organ systems and the accumulation of oxidative damages is the main driving force in the aging process. This disruption of the cell redox balance is associated with the activation of inflammatory pathways linked to senescence and apoptosis. Interestingly, SuperOxide Dismutase (SOD) levels significantly decrease with aging, making cells more vulnerable to oxidative and inflammatory events. As the first line of antioxidant defenses, SOD protects cells from oxidative damages, and a stimulation of SOD expression has been demonstrated to increase life expectancy of several organisms. Boosting its body's SOD levels represents an efficient strategy to prevent cell damages and slow down aging.

The free radical theory of aging

Denham Harman has first proposed the free radical theory of aging in the 1950s, postulating that damage to cellular macromolecules via free radical production in aerobic organisms is a major determinant of life span[1]. Today, there is strong evidence that an accumulation of Reactive Oxygen Species (ROS), especially superoxide anions ($O_2^{\bullet -}$), and oxidative damages are key contributors of the aging process in cells and tissues (Figure 1)[2]. A progressive and irreversible accumulation of oxidative damages contributes to impaired physiological function, increased incidence of age-related disorders, and reduced life span[3, 4]. Studies with animal models have shown that longer-lived animals show reduced oxidative damage and/or increased resistance to oxidative stress[4].

Aging & inflammatory pathways

An age-related disruption in intracellular redox balance appears to be a primary causal factor in producing a chronic state of inflammation. Besides impairing a cell's ability to effectively remove ROS, this redox imbalance leads to an activation of redox-sensitive transcription factors[3]. Overall, the redox modification of transcriptional factors leads to the activation or inactivation of signaling pathways that will subsequently produce changes in gene expression profiles, including those affecting cellular proliferation, differentiation, senescence, and death (Figure 1)[3].

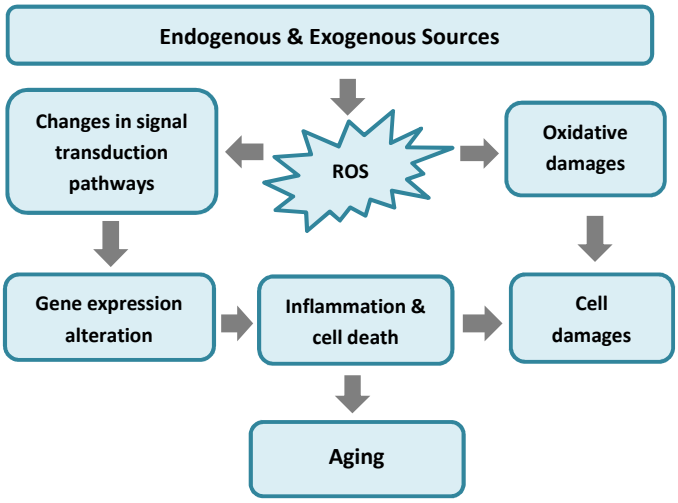

Figure 1: Aging: a ROS-dependent process[3].

An SOD depletion accelerates aging

Lifespan evolved with the ability of organisms to cope with damaging free radical reactions. One of the main assumptions of the free radical theory is that normal antioxidant defense levels are not sufficient to scavenge the excess of ROS produced. Aging results from the alteration of antioxidant enzyme levels, especially SOD, which enhances oxidative stress and elicits cell oxidative damage[5].

In yeast, lifespan is shortened by deleting both Cu,Zn-SOD and Mn-SOD[6]. Further investigations have shown a significant shortened life expectancy (-80%) in *Drosophila* lacking Cu,Zn-SOD[7]. Similarly, SOD depleted mice have a 30% reduction in means life span and a 40% in maximum life span[8].

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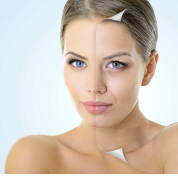

This correlation has been clinically confirmed on humans. People with Down syndrome have an altered SOD/Glutathione Peroxidase ratio, leading to premature aging[9]. Several studies have demonstrated that there are age-related decreases in SOD activity in human erythrocytes. In a Polish population aged between 4 and 80 years old, a significant depletion of SOD erythrocyte activity by 14% and 11% has been observed in old people compared to young and middle ones respectively (Figure 2)[10].

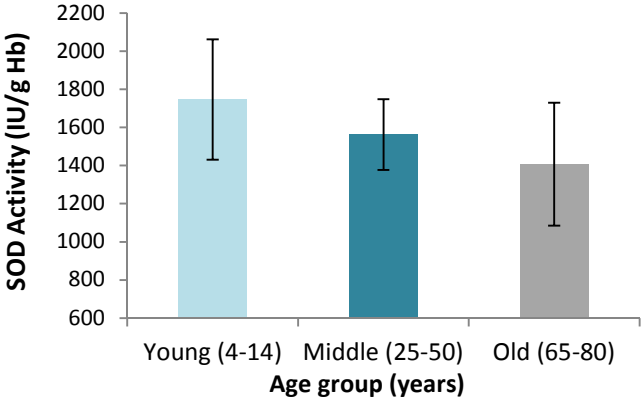

Figure 2: SOD activity in erythrocytes as function of age[10].

Surprisingly, the decline in SOD begins from the age of 18 and is maintained until the old age, as observed by an investigation performed on a Spanish population (Figure 3)[11].

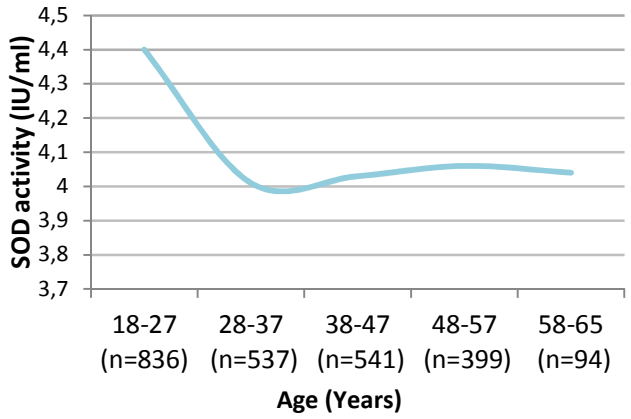

Figure 3: Impact of aging on SOD levels[11].

Interestingly, this depletion of SOD activity continues to increase even in people aged of 60 and higher. Authors have reported a significant decrease of SOD levels in 41 centenarians by -20% compared to the group of elderly subjects[12]. The reduced SOD levels observed with aging leads to an exacerbation of age-related disorders.

SOD: an anti-aging agent

As the first line of antioxidant defenses, SOD helps to protect cells from oxidative damages[13]. SOD also exhibits well-established anti-inflammatory effects, preventing the activation of senescence pathways[14].
Many reports have studied the effect of an SOD induction on longevity in different organisms. The life expectancy of yeast has been reported to be increased by overexpressing Mn-SOD[15]. Other investigations report that overexpression of both Cu,Zn-SOD, Mn-SOD and catalase significantly increases the lifespan of *Drosophila*[16]. Similarly, transgenic mice overexpressing Mn-SOD have shown an 18% increase in maximum life span[17]. In the 1980s, it has been observed that mammals which produced higher tissue and serum SOD levels live longer than those with lower SOD levels[18, 19]. Boosting its body SOD levels represents an efficient anti-aging strategy.

It is scientifically proven that aging results from an accumulation of ROS and oxidative damages. This disruption of the redox balance leads to inflammatory events and a significant depletion in SOD levels. Aged people have significantly lower SOD levels than younger population. The decline in SOD levels begins in young adults and is maintained until the old age. As the first line of antioxidant defenses, a restoration of SOD levels is efficient in preventing cell aging by:

- **Balancing the ROS production**
- **Preventing oxidative damages**
- **Inhibiting inflammatory reactions**
- **Avoiding cell death**

Thanks to its potent antioxidant action, a restoration of SOD levels leads to a significant increased life span.

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