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A Summary of Research on Anti-aging from Genetic Perspective

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Abstract: As people age, the risk of diabetes, cardiovascular disease, cancer and neurodegenerative diseases increases, and globally, with the continuous improvement of living standards, people's life expectancy is also increasing, so how to enjoy a healthy old age, more and more attention, how to delay aging is a matter of concern. Anti-aging drugs were named one of the top ten breakthrough technologies in the world by MIT Technology Review in 2020. This paper elaborates on the progress of anti-aging research and summarizes it to provide reference for anti-aging theoretical research.

Keywords: Anti-aging; Gene; Review.

1. Overview

Aging refers to the degeneration of cells, tissues and organs in structure and function after the body develops and matures, and is a spontaneous biological process caused by the interaction of various complex factors such as age, genetics and environment [1]. From a macroscopic point of view, the aging body is slow to move, hair is sparse and white, skin is loose and age spots appear, vision and hearing are reduced, memory ability is reduced, organ function is impaired, immunity and metabolism are low; Microscopically, senescent cell membrane permeability increases, the number of organelles decreases, and abnormal substances such as lipofuscin are deposited intracellularly, eventually leading to apoptosis [2]. Although aging is not a disease, this degenerative process has led to the occurrence and development of many aging-related diseases such as atherosclerosis and Alzheimer's disease [3], and a variety of common clinical complications such as infarction and embolism caused by these diseases are high causes of death in the elderly. In addition, affected by environmental pollution, increased work pressure and bad living habits, modern people have premature aging, which seriously affects people's quality of life. Therefore, finding ways to delay aging is not only an effective way to fight aging-related diseases, but also has great significance for saving medical costs and improving the quality of human life. Exploring the mechanisms related to aging and finding ways to delay aging has become an urgent topic in modern scientific research.

2. Progress in Anti-aging Research

2.1. Calorie Restriction

Caloric restriction (CR) refers to the restriction of an organism's total daily energy intake while ensuring that it receives sufficient nutrients. A large number of studies have proved that CR is currently the most effective means of extending the lifespan of model organisms [4]. Long-term CR can regulate body metabolism, delay physiological aging process, and reduce the incidence of various aging-related diseases such as cardiovascular disease and type II diabetes [5]. It is believed that CR may delay aging by reducing energy metabolism, thereby reducing oxidative stress levels, improving oxidative damage accumulated with age, and thus delaying aging. Although experiments have proved that CR can delay aging, there are certain risks in implementing CR in people with metabolic diseases, and there is no unified implementation standard, which is difficult to ensure the safety and efficacy of CR. On the other hand, CR requires perennial dietary restrictions, which is difficult to implement and also limits the application of CR.

2.2. Chemical Drugs

Metformin is a commonly used clinical treatment drug for type II diabetes, and studies have found that metformin can effectively extend the life span of a variety of model organisms, and clinical experiments have shown that metformin can reduce the incidence of cardiovascular disease, dementia and other aging-related diseases [7]. Rapamycin is an immunosuppressant, and the study found that rapamycin can not only delay the physiological aging process of model organisms, but also improve a variety of aging-related characteristics, and have good anti-aging effects, but will cause various side effects such as hematopoietic system dysfunction and metabolic disorders. Chlorophenoxyphen is a synthetic antioxidant that has the effect of stimulating the central nervous system. Studies have found that chlorophenoxyphen can inhibit the activity of a variety of oxidases in the body, remove lipofuscin in nerve cells, and can be used to treat diseases such as senile dementia. Clinical studies have shown that the Nrf2 agonist Otipra can effectively delay the aging rate of mesenchymal stem cells in children with Progeria, but there are many adverse reactions, such as nausea, vomiting, abdominal pain, etc., and in more serious cases, abnormal sensations of the extremities will occur [6]. Although chemical drugs have been found to have certain anti-aging effects, the side effects caused by them limit their clinical application.

2.3. Traditional Chinese Medicine Compound

Yang Jing et al. studied the effect of Sijunzi decoction on aging model mice by establishing a D-galactose aging model, and found that Sijunzi decoction can improve the learning and memory ability of aging mice, improve antioxidant enzyme

activity in brain tissue, reduce the content of MDA in various tissues, improve telomerase activity in heart and brain tissues, and prevent mtDNA deletion mutations in hippocampal cells of aging mice. Wu Qian et al. used two models of drosophila and D-galactose-induced aging mice to study the anti-aging effects of Liuwei Dihuang decoction and its tonic and laxative components, and found that Liuwei Dihuang decoction could prolong the survival of fruit flies, improve the antioxidant capacity and tissue telomerase activity of aging mice, and the three complementary components could prolong the survival of fruit flies and improve the tissue telomerase activity of aging mice. Tridiarrheal components can reduce the serum MDA content of aging mice. Therefore, it is believed that Liuwei Dihuang soup and its tonic and laxative components improve the body's anti-aging ability through different ways [7]. Xia Huaying et al. observed the effect of Zuogui Pill on D-galactose-induced aging rats, and found that Zuogui Pill can play a role in delaying aging by improving the antioxidant capacity of aging rats and reducing lymphocyte DNA damage. Ko Kam et al. found that the Chinese herbal formula Vigconic 28 (i.e., Wellcome capsules, the main ingredients of ginseng, deer antler velvet and dodder seed) may delay the aging of mice by increasing the activity of antioxidant enzymes in the body. In addition, Jinkui Kidney Qi Pill, Shengmai San, Qing Palace Changchun Dan, etc. all have anti-aging effects.

2.4. Natural Medicine

(1) Flavonoids and polyphenolic compounds

Studies have found that the administration of apigenin to aging mice can increase SOD activity, reduce MDA content, and significantly improve the learning and memory ability of aging mice. In vitro tests have shown that apigenin can induce human skin fibroblasts to synthesize collagen and delay skin aging. Further studies have shown that the anti-aging effects of apigenin are associated with activating the Nrf2 pathway and inhibiting inflammatory aging. Alugoju et al. found that combination therapy with calorie restriction and quercetin can effectively delay aging. In addition, it was found that quercetin and its derivative quercetin octanoate can induce the expression of antioxidant-related proteins and increase antioxidant levels, thereby delaying the aging of human skin fibroblasts. Rutin can exert anti-aging effects by scavenging excess free radicals and inhibiting cellular lipid peroxidation. In addition, naringin, luteolin, puerarin and troxerutin can also play a role in delaying aging. In addition to flavonoid monomers, many effective parts of flavonoids have also been shown to have anti-aging effects. Soy flavonoids can significantly increase the antioxidant enzyme activity, reduce the peroxide content, and significantly increase the hydroxyproline content in skin tissue, which has certain anti-aging effects. Lockyang flavonoid extract can extend the average and maximum lifespan of adult female flies and improve the reproductive ability of female flies, and its anti-aging mechanism may be related to reducing free radical formation and removing excess free radicals in the body [8]. Total flavonoids can effectively increase the collagen content of skin tissues of aging mice, increase the activity of a variety of antioxidant enzymes, reduce the content of MDA, and increase the expression of Sirt1 and CyclinD1, reduce the expression of p16 and p21, and delay skin aging. In addition, sea buckthorn total flavonoids, epimedium total flavonoids, ginkgo biloba flavonoids, etc. all have anti-aging effects.

(2) Polysaccharide compounds

Salidroside is the main active ingredient of Rhodiola, which has various effects such as regulating immunity and delaying aging. Mao Genxiang et al. showed that salidroside can prolong the lifespan of fruit flies, improve the nervous system and immune system of D-galactose aging model mice, reduce the level of AGEs, and have a good effect on the treatment of aging-related osteoporosis. Li Hui et al. speculated that salidroside may improve oxidative stress by activating the PI3K/Akt/Nrf2/HO-1 signaling pathway, thereby delaying neurosenescence. Mao et al. found that salidroside was able to reverse H2O2-induced premature aging of human fibroblasts. In addition, studies have found that salidroside also has a role in skin aging. Numerous studies have shown the potential of salidroside to develop as an anti-aging drug. Zhang Limei et al. established a D-galactose-induced aging rat model to study the anti-aging effect of purple yam polysaccharides, and found that purple yam polysaccharides can improve the organ index of aging rats, enhance the antioxidant capacity of various tissues, and downregulate the expression of p53 and p21 proteins, thereby exerting anti-aging activities. He Dan et al. gave amber polysaccharide to natural aging mice, and found that sheep polysaccharide could increase the expression of Nrf2 in the liver of aging mice, thereby improving the antioxidant capacity of aging mice, thereby delaying aging. Cheng et al. found that angelica polysaccharides can delay brain tissue aging by increasing antioxidant capacity, reducing the level of inflammatory factors, and downregulating the expression of p53 and p21 proteins in nerve cells [9]. Duan Yihan et al. studied the anti-aging effect and mechanism of agaricus blazei polysaccharide on D-galactose-induced aging mice, and found that agaricus blazei polysaccharide can improve the learning and memory ability of aging model mice, and its anti-aging mechanism may be related to the regulation of Keap1/Nrf2/ANE signaling pathway. In addition, a variety of polysaccharide components such as seaweed polysaccharides and codonopsis polysaccharides also have anti-aging effects.

(3) Vitamins

Vitamin E is a natural fat-soluble antioxidant used clinically to delay aging and improve immunity. Studies have found that vitamin E can delay aging by scavenging free radicals, protecting the body's immune system, promoting RNA and protein biosynthesis, and promoting human energy metabolism. In addition, studies have shown that vitamin E can improve cholesterol deposition, thereby reducing the incidence of various aging-related diseases such as atherosclerosis, coronary heart disease, and cerebral vascular sclerosis. Vitamin C is a natural water-soluble antioxidant. Studies have shown that vitamin C has the effect of improving atherosclerosis and reducing the incidence of coronary heart disease. The study found that vitamin C exhibited anti-aging effects in an in vitro-induced human cardiomyocyte aging model. Inositol is a vitamin in the B vitamin group, and the study found that inositol can increase the relative expression of antioxidant enzyme genes in the liver tissues of D-galactose aging mice, significantly improve the antioxidant capacity of aging mice, and thus play an anti-aging role. In addition, studies have found that vitamin A, vitamin B1, and vitamin D also have antioxidant and anti-aging effects [10].

(4) Other ingredients

Ursolic acid is a triterpenoid compound found in a variety of plants. Studies have proved that ursolic acid is a strong antioxidant that can effectively scavenge free radicals and protect DNA from oxidative stress, thereby exerting anti-aging effects. Carotenoids are widely found in fruits and

vegetables. Studies have found that feeding lutein can enhance the antioxidant enzyme activity in fruit flies and prolong the average life span of fruit flies. Engler et al. believe that β-carotene can prevent aging and the occurrence of various aging-related degenerative diseases. Zhang Zhuhai et al. found that β-carotene can improve the reproductive ability and prolong the lifespan of fruit flies, and β-carotene can also improve the antioxidant capacity of aging rats and delay aging in rats. Melatonin is an amine hormone secreted by the pineal gland that has a strong antioxidant effect and can protect the body from free radical damage. With age, the secretion of melatonin gradually decreases, and supplementation with exogenous melatonin can effectively delay aging [11]. Ubiquinol 10 may delay age-related hearing loss and prevent the onset of aging by increasing levels of SIRT1, PGC-1α, and SIRT3.

3. Summary

With the development of life sciences, scholars have discovered that the aging mechanism has complex, multifactorial, and comprehensive characteristics, and have proposed various theories such as free radical theory, inflammatory aging theory, and cell apoptosis theory. The free radical theory was proposed by Harman in 1956 and is currently the most recognized theory of aging. It believes that excessive free radicals produced by environmental and self-factors are the cause of aging in the body. The kIotho gene is located at 13q12, with a total length of 50 kb, containing four Intron and five Exon. There is no typical TATA box or CAAT box in the promoter region, but there are five SP1 binding sites. The function of intracellular and extracellular NAMPTiNAMPT as a NAD+biosynthetic enzyme has been fully established, while the physiological correlation and function of eNAMPT have long been controversial.

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