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Research Article

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Harnessing Longevity Genes for Lifespan Extension: Insights from Naked Mole Rats

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Abstract

As we grow older. Experience the cycle of life's changes, in our bodies and health over time leading to our inevitable passing away from this world someday that we all share as humans together through the generations that have come before us and will come after us too. Illnesses like cancer or heart conditions or brain degeneration that become more frequent as we get older can have an impact. Make life harder as we reach our later years beyond what is considered middle age by most standards these days. Although most people can expect to live about 80 to 90 years based off what we know from studying populations throughout time around the globe where humans have lived and thrived together in communities small. Scientists are now looking at how our genetic makeup might play a role, in living lives than expected by examining how certain genes may contribute to longevity beyond what's typically seen in the general population. One interesting group being studied for their ability to resist the effects of aging are mole rats who seem to defy expectations by showing signs of age related diseases despite their advanced years compared with other animals studied so far. This article delves into high molecular weight hyaluronic acid (HMW HA), from naked mole rats (NMRs) can extend the lifespan of genetically modified mice significantly. Recent research indicates that introducing the hyaluronan synthase. 2 Gene from mole rats improved the health span and increased the lifespan of mice by 4.4%. These results demonstrate the potential of using elements from living species to create interventions that could slow down aging and related diseases in humans. This review emphasizes the importance of studies, in biogerontology.

Keywords: Aging, Longevity Genes, Naked Mole Rats, High Molecular Weight Hyaluronic Acid, Lifespan Extension, Age-Related Diseases

Highlights

- Explores genes that enhance longevity and combat age-related diseases.
- Naked mole rats show exceptional resistance to aging diseases like cancer and arthritis.
- High molecular weight hyaluronic acid (HMW-HA) from mole rats extended mice lifespan by 4.4%.
- This study reveals potential for genetic interventions to prolong human healthspan.

1. Introduction

Aging is an intricate and inevitable biological process that results in the gradual decline of an organism's physiological functions, ultimately leading to death. With aging comes an increased susceptibility to a wide range of diseases, including cancer, cardiovascular diseases, and neurodegenerative disorders [1]. This natural process affects all living organisms, but the rate at which it occurs and the lifespan of different species vary significantly. In the natural world, we observe a wide spectrum of lifespans:

some species live for only a few days or weeks, while others can survive for centuries. For example, certain species of turtles and whales have been documented to live for more than 200 years [2]. In humans, the average lifespan typically falls between 80 and 90 years, though this is influenced by various factors such as genetics, lifestyle, and environmental stressors [3]. Over the last century, improvements in healthcare, nutrition, and sanitation have significantly increased human life expectancy in many parts of the world. However, recent trends suggest that environmental challenges, lifestyle choices, and the growing prevalence of chronic diseases could lead to a stagnation or even a decline in the average lifespan [4]. The pressing issue of aging-related diseases, especially in aging populations, has driven extensive research into understanding the biological mechanisms underlying aging.

One of the most striking observations in the study of aging is the significant variation in longevity across species. While humans are considered to have an intermediate lifespan, there are animals that show exceptional longevity and resistance to diseases typically associated with aging. These animals have garnered the attention of researchers who aim to understand the genetic and molecular pathways that enable such resistance. Among these species, the naked mole rat (NMR) has emerged as a model organism of interest due to its remarkable longevity and unique resistance to many age-related diseases [5]. The naked mole rat is a small, subterranean rodent native to East Africa. Despite its modest size and unassuming appearance, it is one of the longest-lived rodents, with a lifespan of over 30 years. What makes the NMR particularly intriguing to researchers is its resistance to many of the diseases that afflict other mammals as they age, including cancer, cardiovascular diseases, and neurodegenerative disorders (Lewis et al., 2016). This exceptional resilience suggests that the NMR possesses unique biological mechanisms that protect it from the detrimental effects of aging. Cancer resistance in NMRs is one of the most well-documented and remarkable features of their biology. While cancer is one of the leading causes of death in humans and other animals, it is extremely rare in NMRs. Studies have shown that NMR cells are hypersensitive to contact inhibition, a process that halts cell growth when cells become too crowded, thus preventing the uncontrolled cell proliferation that leads to tumor formation [6]. Additionally, NMRs produce a unique form of hyaluronan, a substance found in connective tissues, which plays a role in preventing cancer by inhibiting cell growth and promoting tissue elasticity [7].

Beyond cancer resistance, NMRs also exhibit resilience to cardiovascular diseases. Cardiovascular diseases are a leading cause of mortality in aging humans, primarily due to the buildup of plaques in arteries, known as atherosclerosis, and the stiffening of blood vessels. NMRs, however, show little to no signs of these conditions as they age, suggesting that they possess protective mechanisms against cardiovascular decline (Lewis et al., 2016). Understanding these mechanisms could provide valuable insights into preventing or mitigating age-related cardiovascular diseases in humans. Another area where NMRs excel is in their resistance to neurodegenerative disorders. In humans, diseases like Alzheimer's and Parkinson's become increasingly common with age, characterized by the progressive loss of neurons and cognitive decline. NMRs, despite their long lifespans, show no signs of such neurodegeneration [8]. It is hypothesized that their brains are protected by mechanisms that reduce oxidative stress and enhance protein quality control, both of which play critical roles in maintaining neuronal health [9]. The study of NMRs and their exceptional longevity offers a promising avenue for understanding the biological processes that govern aging and disease resistance. Researchers hope that by identifying the genetic and molecular pathways responsible for the NMR's resilience, they may be able to apply this knowledge to human biology. One potential avenue for intervention is through the manipulation of genes involved in DNA repair, oxidative stress, and protein homeostasis—areas where NMRs appear to have superior capabilities compared to other mammals [10]. The insights gained from studying long-lived species like NMRs could have profound implications for human health and longevity. With the global population aging at an unprecedented rate, the burden of agerelated diseases is becoming an increasingly pressing public health issue [11]. By uncovering the biological secrets of species that have evolved to resist aging and its associated diseases, scientists hope to develop therapies that can extend human health span—the period of life free from chronic diseases—rather than merely prolonging lifespan. This distinction is crucial, as the goal is not only to help people live longer but to ensure that these additional years are spent in good health. In conclusion, aging is a universal biological process that manifests differently across species. While humans face a growing challenge in managing age-related diseases, certain animals like the naked mole rat exhibit remarkable resilience to these conditions. By studying the biological mechanisms underlying their longevity and disease resistance, researchers aim to uncover new strategies for promoting healthy aging in humans. As our understanding of the genetics and molecular biology of aging advances, the possibility of extending both lifespan and health span becomes an exciting frontier in biomedical research.

1.1. Longevity Mechanisms in Naked Mole Rats

The unique biology of NMRs has led to various investigations into their longevity and disease resistance mechanisms. Recent studies have focused on high molecular weight hyaluronic acid (HMW-HA), a substance found in NMRs that plays a crucial role in cellular repair, anti-inflammatory responses, and tissue protection [7]. HMW-HA has been identified as a key factor contributing to NMRs' resistance to cancer and other age-related diseases, positioning it as a target for research into lifespan extension. To explore the potential benefits of HMW-HA, researchers from the University of Rochester conducted a groundbreaking experiment where they transferred the naked mole rat hyaluronan synthase-2 gene into mice [7]. This gene is responsible for the production of HMW-HA in NMRs. The study aimed to determine whether introducing this gene into mice could extend their lifespan and improve overall health.

1.2. Experimental Findings

The results of this experiment revealed several significant outcomes. Mice that expressed the NMR hyaluronan synthase-2 gene exhibited notable improvements in health markers, including enhanced tissue repair and reduced inflammation. Most importantly, these genetically modified mice experienced a 4.4% increase in median lifespan compared to control mice, demonstrating the potential of this genetic modification in promoting longevity [7]. These findings suggest that the biological mechanisms responsible for NMRs' exceptional longevity can be harnessed to enhance the lifespan and healthspan of other mammals. The implications of this research are profound, as they open up new avenues for addressing age-related diseases and promoting healthy aging through genetic interventions.

2. Discussion

The discovery that the introduction of NMR-derived HMW-HA genes can extend lifespan in mice represents a significant advancement in the field of biogerontology. It underscores the potential of leveraging natural longevity mechanisms to develop therapeutic interventions for humans. Moreover, this research aligns with the growing interest in genetic modifications and their role in delaying aging and preventing age-related diseases [12]. While the 4.4% increase in lifespan observed in mice is modest, it marks a critical first step toward understanding how genetic factors from long-lived species can be applied to improve health and longevity in humans. Future research should focus on exploring additional longevity genes and mechanisms in NMRs and other long-lived species. By doing so, scientists may unlock further insights into the aging process and develop strategies to mitigate its impact on human health.

3. Conclusion

The introduction of NMR-derived longevity genes into mice represents a promising approach to extending lifespan and combating age-related diseases. This review highlights the potential of high molecular weight hyaluronic acid (HMW-HA) and its associated gene, hyaluronan synthase-2, in promoting healthy aging. The success of this experiment underscores the importance of continued interdisciplinary research in biogerontology, which may one day lead to the development of therapies that not only extend lifespan but also improve the quality of life in aging populations. With further research, the biological secrets of longlived species like NMRs could pave the way for breakthroughs in human health and longevity [13].

Author Contributions

All the authors contributed equally.

Declarations

Conflict of interest: The authors declare that there is no Conflict of interest.

Ethical approval: Not needed

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