KLOTHO GENE THERAPY AS A SINGLE-DOSE ANTI-AGING STRATEGY: A MOUSE MODEL STUDY DEMONSTRATING LIFESPAN AND HEALTHSPAN EXTENSION

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Mini Review

Klotho Gene Therapy as a Single-Dose Anti-Aging Strategy: a Mouse Model Study Demonstrating Lifespan and Healthspan Extension

Ata Şah*

For affiliations and correspondence, see the last page.

Abstract

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Abstract

Recent research by Spanish scientists has introduced a promising anti-aging intervention via gene therapy using the Klotho protein. In aging mice, a single administration of Klotho resulted in nearly a 20% increase in lifespan and significant improvements in muscle, bone, and brain function. This systemic effect demonstrates Klotho's potential as a master regulator of aging. Mice treated at 12 months exhibited a lifespan increase equivalent to human life extending from 80 to 96 years. Although translation to humans remains under investigation, this breakthrough paves the way for gene-based longevity strategies. Additionally, it is noted that elevated vitamin D levels suppress Klotho expression, prompting consideration for targeted vitamin D management in future therapies.

1. Introduction

Aging is an inevitable biological process characterized by progressive deterioration in physical and cognitive function, often leading to chronic diseases. As the global population ages, there is a critical need to develop interventions that not only extend lifespan but improve quality of life. Klotho, an anti-aging protein discovered in 1997 by Kuro-o et al. [1], has shown significant promise in animal studies due to its regulatory role in multiple physiological pathways, including oxidative stress, mineral homeostasis, insulin signaling, and neurogenesis.

2. Methods

In the recent study conducted by a Spanish research team [3], a **viral vector-based gene therapy** was utilized to deliver the Klotho gene systemically to 12-month-old mice. This single administration enabled persistent expression of the Klotho protein over time. Control mice received a placebo treatment. Klotho Gene Therapy

3. Results

3.1 Lifespan Extension

Treated mice lived, on average, 5 months longer than the untreated group — a 20% increase in lifespan, which translates in human terms from 80 to 96 years.

3.2 Musculoskeletal Improvements

Mice exhibited improved grip strength, coordination, and endurance. Muscle tissues showed less fibrosis and better regeneration. Fountain of youth

3.3 Bone Density and Activity

Bone scans of female mice indicated stronger bones and higher osteoblast activity, implying increased bone-building capacity.

3.4 Neurological and Cognitive Benefits

Brain analyses revealed increased neurogenesis, improved mitochondrial function, enhanced autophagy, and a more balanced immune environment.

4. Discussion

These findings demonstrate the **multisystemic impact** of Klotho, making it one of the most promising candidates for anti-aging therapies. By acting at a genomic level to restore cellular homeostasis, Klotho influences not just one organ but the overall physiology of aging. This study confirms that gene therapy targeting Klotho is capable of significantly improving both lifespan and healthspan in mammals.

An additional consideration arises regarding **vitamin**

D. High serum levels (>50 ng/mL) may **inhibit Klotho expression** [2], which could reduce the effectiveness of Klotho-based treatments. Thus, balancing vitamin D intake may be necessary in clinical applications of this therapy.

5. Conclusion

Klotho-based gene therapy represents a pivotal shift in anti-aging science, moving from isolated organ treatments to a **systemic approach**. While this study is limited to animal models, its translational potential is immense. Future human trials, ethical review, and nutrient-gene interaction models will be essential to move forward. The findings support the integration of Klotho therapies into future longevity medicine and geroscience interventions.

6. References

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2. Brownstein, A.J., et al. (2020). Vitamin D suppresses Klotho expression in kidney cells: implications for aging. *Aging Cell*, 19(2), e13053. https://doi.org/10.1111/acel.13053

3. [Spanish Research Team Study on Klotho, 2025 — DOI to be added upon sciMatic publication]

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7. Conflict of Interest

The author declares no conflict of interest.

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References

Affiliations and Corresponding Informations

Corresponding: Ata Şah
Email:
Phone: 05060568409

Ata Şah:
Muğla