BIOMEDICAL SCIENCE JOURNAL FOR TEENS

OCTOBER 2022

What can we learn about aging from naked mole-rats?

Authors:
Chris Faulkes, Steve Horvath, Vera Gorbunova and others

Associate Editors:
Allison Gamzon and Alexandra Appleton

Abstract

Did you know that naked mole-rats don't age the same way humans and other mammals do? These incredible rodents don't seem to age physically and they are resistant to age-related diseases. That's why they can live over 30 years! Scientists are trying to understand how aging works in naked mole-rats so that they can better understand aging in humans. We conducted a DNA analysis of naked mole-rat tissue to find out if their DNA shows signs of aging. We discovered that naked mole-rats do age on a molecular level like other mammals. Identifying where the DNA changed in naked mole-rats allowed us to predict what effects these changes might have on the body. We also found that members of a naked mole-rat community age faster than their queen.

Introduction

Naked mole-rats are not your typical rodent. Unlike other mammals, they are **eusocial**. That means they live in colonies with a social structure like bees and ants. They have a queen that breeds with a few select males, while the other members of the colony work to support the colony and don't breed at all. Naked mole-rats are also interesting because they live long lives compared to rodents of similar size. They can live up to 37 years, as compared to mice, who only live up to 4 years. They also don't experience age-related **physiological** changes and they are resistant to age-related diseases. That's why these animals are so interesting to scientists studying aging.

Naked mole-rats, like all organisms, have **DNA**. DNA is the code that carries information about an individual. Researchers have found that with aging, DNA undergoes **methylation**. That means that **methyl groups** ($—CH_3$) are added to DNA over time. These methyl groups are typically added at specific locations along the DNA code. Scientists call these locations **CpGs**.

Fun fact: Naked mole-rats don't drink water! Instead, they get all the hydration they need from their plant-based diet.

Photo: Lorna Faulkes Photography

Scientists have been able to use the methylation of DNA to create a biological clock that can indicate an individual's molecular age. They call this an **epigenetic clock**. These clocks are very accurate for mammals, including humans. Because naked mole-rats age differently than other mammals, we created epigenetic clocks for them. We then used these clocks to see what happens to them as they age. We also looked at how the aging of a typical naked mole-rat compares to that of the queen

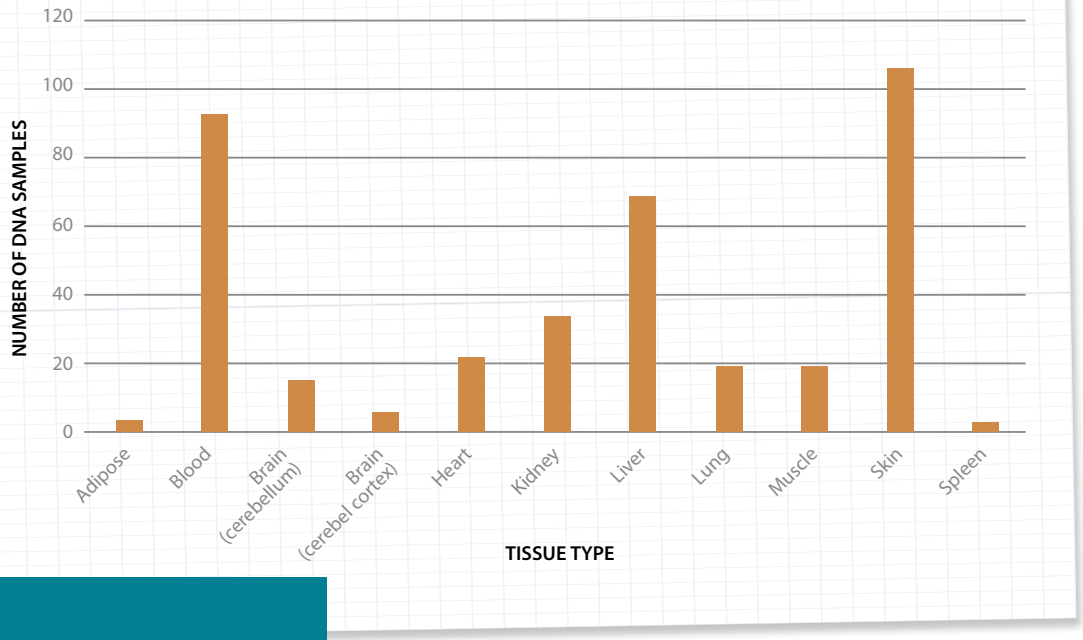
Methods

From our archive of post-mortem samples preserved in our freezers, we collected 11 different tissue samples from naked mole-rats that ranged in age from 0 to 26 years old. From these 11 tissue samples, we obtained 382 DNA samples (Figure 1). We analyzed these samples for DNA methylation. Then we created epigenetic clocks by correlating the age of the animal with the amount of DNA methylation. That means we created a mathematical model that relates DNA methylation with the actual age of the naked mole-rat.

We initially created four epigenetic clocks. We designed each one for a specific type of tissue: blood, kidney, liver, and skin. We also created another epigenetic clock that is a more general clock for all tissues. Then we tested the clocks to make sure that they accurately determined the age of a naked mole-rat. Once we were confident in these epigenetic clocks, we created two clocks that used some of the data to reflect aging in naked mole-rats and humans. Then we looked closely at the DNA to determine which CpGs experienced methylation for naked mole-rats.

Finally, we analyzed 18 blood samples and 4 skin samples from different naked mole-rat queens. We also analyzed samples from non-breeding males and females. Then we used our epigenetic clocks to compare the rate of aging in queens to non-breeding naked mole-rats.

Figure 1: The number of DNA samples obtained from each tissue type.



Why do you think the scientists created epigenetic clocks for blood, liver, kidney, and skin tissues, but not the other tissues?

Results

We created 5 accurate epigenetic clocks for naked mole-rats and 2 for naked mole-rats and humans. These clocks showed that naked mole-rats experience DNA methylation with age. Depending on the location of the CpG, the amount of methylation either increased or decreased. We found that the CpGs most associated with age also became more methylated with age.

We also learned that queens age more slowly than non-breeding naked mole-rats. When comparing CpGs for queens and non-breeding naked mole-rats, we found 237 age-related CpGs that are different. They have different methylation patterns.

Discussion

From our research, we learned that even though it seems like naked mole-rats don't age, they do experience epigenetic aging like other mammals. Other studies show that certain health conditions occur when there is fast epigenetic aging. Since naked mole-rats don't appear to age physically, they aren't getting these health conditions. Why? It is possible that their bodies have figured out ways to prevent the health conditions associated with epigenetic changes. We need to do more research to figure out why the two types of aging don't match.

Our analysis of CpGs helped us determine where DNA methylation occurred. It also helped us to predict how this DNA methylation might affect what happens inside the body of a naked mole-rat. Similarly, the comparison of queens and non-breeding naked mole-rats also helped us **hypothesize** why queens age at a slower rate. With more research, scientists can figure out how lifestyle affects the aging process in naked mole-rats.

Studying aging in this animal is an important way to understand aging in humans. That's why the naked mole-rat-human epigenetic clocks we created will be useful for future research. These clocks will allow scientists to translate their findings in naked mole-rats to humans.

Conclusion

Scientists like us hope that by understanding aging in naked mole-rats, we can understand aging in humans. Hopefully, we can figure out how these creatures avoid the health conditions associated with aging. While we continue our research, you can stay healthy by eating nutritious foods, such as pulses, fruit and vegetables. These foods provide your body with the vitamins and minerals it needs to stay healthy. You also want to be active, get plenty of rest, and maintain a positive attitude whenever you can. Taking good care of your mind and body can help you stay healthy as you age.

Glossary of Key Terms

CpGs – locations on a DNA molecule where methylation can occur.

DNA – a complex molecule present in living organisms that carries genetic information which can be passed onto offspring.

Epigenetic clock – a mathematical model that correlates the amount of DNA methylation in a tissue to the age of the organism.

Eusocial – a social structure common in ants and bees made up of a queen that produces offspring and a community of non-breeding individuals that help.

Hypothesize – to give a possible but not yet proven explanation for something (a hypothesis).

Methyl group – a small molecule that is made up of one carbon atom and three hydrogen atoms (—CH_3).

Methylation – the addition of a methyl group to a protein or to DNA.

Physiological changes – changes related to how an organism or a body part functions.

Acknowledgment: This article's adaptation was supported by the GM Foundation.

Check your understanding

1. Why do we study naked mole-rats to better understand aging?

---

2. What happens to a mammal's DNA as it ages?

---

3. We identified two areas about naked mole-rats and aging that will require more research. Which area do you think we should research next? Explain your choice.

---

4. With a partner or small group, brainstorm how better understanding aging in naked mole-rats could affect humans in the future.

---

5. Research age-related diseases that affect humans. Select one and describe how it impacts a person. Share your research with your classmates.

REFERENCES

Steve Horvath, Amin Haghani, Nicholas Macoretta, Julia Ablaeva, Joseph Zoller, Caesar Li, Joshua Zhang, Masaki Takasugi, Yang Zhao, Elena Rydkina, Zhihui Zhang, Stephan Emmrich, Ken Raj, Andrei Seluanov, Chris Faulkes, and Vera Gorbunova. (2022) *DNA methylation clocks tick in naked mole-rats but queens age more slowly than nonbreeders*. Nature Aging.
https://www.nature.com/articles/s43587-021-00152-1

Smithsonian's National Zoo & Conservation Biology Institute: Naked mole-rat.
https://nationalzoo.si.edu/animals/naked-mole-rat

National Human Genome Research Institute: DNA day activity ideas.
https://www.genome.gov/dna-day/get-activity-ideas

We dedicate this article to the memory of Dr. Steve Le Comber.