

LONG-LIVED RATS REVEAL A SECRET: BETTER DNA REPAIR.

Although many factors have been identified as contributing to aging and death—including cellular senescence, genomic instability, telomere attrition, and metabolic decline—a comprehensive and unified theory of aging is still lacking. Among the hallmarks of aging, DNA damage and the gradual accumulation of mutations over time have long been recognized as central mechanisms. Understanding how some species can mitigate these effects provides important insight into the biology of longevity.

In a study by Chen et al. (1), the authors investigated why the naked mole-rat (*Heterocephalus glaber*), an exceptionally long-lived rodent, shows remarkable resistance to aging. They discovered that, unlike in humans and mice, the cyclic GMP–AMP synthase (cGAS) protein in naked mole-rats is more stable and remains bound to chromatin for a longer time after DNA damage, enhancing the recruitment of key repair factors such as FANCI and RAD50. As a consequence, homologous recombination repair efficiency is boosted, cellular senescence is limited, and tissue aging is delayed. Remarkably, introducing naked mole-rat cGAS into fruit flies and aged mice improved health span and reduced aging markers, whereas reverting the four amino acid substitutions abolished these effects.

If, as this work suggests, improving DNA repair mechanisms is crucial for a longer and healthier life—a finding consistent with the mutation accumulation theory of aging—an obvious question arises: why did such efficient DNA repair systems not evolve in humans?

1. <https://www.ncbi.nlm.nih.gov/pubmed/41066557>