Naked mole-rats defy conventions of aging and reproduction

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Female mole rat. Credit: Jedimentat44/flickr/CC BY 2.0

Naked mole-rats live in colonies of two breeders and around 300 non-breeding workers. Although the breeding pair carries the metabolic cost of reproduction and, in the queen's case, lactation, they live longer than non-breeders and remain fertile throughout their lives. Researchers at the Leibniz Institute on Aging in Germany investigated the genetic mechanisms beneath this apparent paradox. Their findings are published in the open access journal *BMC Biology*.

Dr. Martin Bens, the corresponding author said: "Our results indicate that when naked mole-rats mature into breeders, it changes their aging rates, meaning that breeders are able to live longer than non-breeders. This is surprising, as evidence from other species suggest that reproduction, which ensures the survival of the species as a whole, reduces the lifespan of the individual. In naked mole-rats reproduction appears to prolong the breeders' lifespan. This goes against the common expectation that mammals either invest resources in a long life or in reproduction."

The researchers analyzed the transcriptomes—the sum of all transcribed genes—for tissue samples taken from a range of organs, including heart, liver, and gonads. They compared the transcriptomes of naked mole-rat breeders to that of non-breeders, as well as to breeding and non-breeding guinea pigs, which are close relatives of the naked mole-rat but have a shorter lifespan.

The authors found that genes related to aging were expressed differently in samples from breeding naked mole-rats than those from guinea pigs and non-breeding naked mole-rats. For example, a gene related to muscle regeneration showed higher expression in naked mole-rat breeders which may be linked to higher resistance to muscle loss during aging. Gene expression changes like this may contribute to the exceptionally long lifespan of naked mole-rat breeders.

Dr. Bens said: "Unlike non-breeding guinea pigs and other rodents, non-breeding naked mole-rats are not sexually dimorphic; they show no differences in body size, body mass or external genitalia, as well as few behavioral differences. One of the main and surprising findings of our study is that transcribed genes in non-breeding naked mole-rats also show no significant differences between females and males. However, we found that the transcriptome changes significantly when they mature into breeders."

When the authors separated non-breeding naked mole-rats from colonies and paired them with naked mole-rats of the opposite sex, the workers transitioned into breeders. The transition was accompanied by physical and behavioral changes that differed between males and females—the animals became sexually dimorphic. Sexual maturation was also associated with a change in gene expression levels linked to extended life and health span.

Dr. Bens said: "Deeper investigations of naked mole-rat transcriptome data can help us understand how sexual maturation is regulated. This could potentially help us better understand sexual maturation in humans, where the onset of puberty varies between individuals and is influenced by a variety of factors such as stress and nutrition. Variations in puberty onset have implications for the risk for diseases such as breast cancer or cardiovascular diseases. Our data may help identify targets to mitigate these variations."

In another study titled 'Species comparison of liver proteomes reveals links to naked mole-rat longevity and human aging,' published in *BMC Biology* on the same day, Dr. Bens and colleagues compared the liver of naked mole-rats with those of guinea pigs to further investigate the molecular mechanisms that underlie naked mole-rat longevity.

Alessandro Ori, the corresponding author of the study said: "We found

that naked mole-rat livers have a unique expression pattern of mitochondrial proteins that result in distinct metabolic features of their mitochondria, including an increased capacity to utilize fatty acids. We were also able to show that similar molecular networks are affected during aging in both naked mole-rats and humans, which suggests that there may be a direct link between these networks and the longevity of these species, both of which would be expected to have much shorter lives based on their body mass."

More information: Martin Bens et al, Naked mole-rat transcriptome signatures of socially suppressed sexual maturation and links of reproduction to aging, *BMC Biology* (2018). DOI: 10.1186/s12915-018-0546-z

Ivonne Heinze et al. Species comparison of liver proteomes reveals links to naked mole-rat longevity and human aging, *BMC Biology* (2018). DOI: 10.1186/s12915-018-0547-y

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