# X chromosome not the reason for sex differences in lifespan

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Researchers at Linköping University, Sweden, use fruit flies as a model organism to study sex differences in lifespan. Credit: Karin Söderlund Leifler / Linköping University

The shorter average lifespan of males compared to females appears not

to be a result of the fact that males have only one X chromosome. This is the conclusion from a research study on fruit flies at Linköping University, Sweden. The results have been published in the scientific journal *Evolution*.

It is common that the lifespans of males and females differ. For mammals, including humans, females live on average somewhat longer than males. The difference in humans at a global level is that women live 4.7 years longer than men, according to statistics from WHO for 2015. We do not know why this is the case in so many species, but several theories have been put forward. Researchers at Linköping University (LiU) have now had a close look at one of the theories concerning the role of genetics in sex differences in lifespan.

One obvious genetic difference between the sexes is that they have different numbers of sex chromosomes, and what is known as the "unguarded X hypothesis" is based on this. In many species, including humans, females have two X chromosomes while males have an X and a Y chromosome. In birds, and in some species of fish, reptiles and insects, males have two copies of the same sex chromosome, and in such cases it is most often males who have the longer lifespan.

The sex that has two X chromosomes has two variants of each gene on the X chromosome. The gene variants act as back-ups for each other, so if a gene on the X chromosome is not functional, the gene copy on the other chromosome can compensate for this. In the sex that has two different sex chromosomes (one X and one Y), in contrast, only one copy of most genes on the X chromosome is present, and no back-up is available if there is something wrong with them. The theory suggests that this mechanism contributes to making the average lifespan of males shorter. It is an old theory, but only a few studies have been carried out to test it. The researchers who carried out the new study used fruit flies (Drosophila melanogaster) to test the theory.

"The fruit fly is a useful model organism to test the hypothesis, since females generally live longer, and the X chromosome constitutes as much as one fifth of the genetic material. If the theory is true, the effects should be clear in the fruit fly," says Martin Brengdahl, PhD student at the Department of Physics, Chemistry and Biology at LiU, and one of the principal authors of the study.

The researchers bred fruit flies in which the two X chromosomes in the females were identical, such that neither of the copies was able to compensate for faults in the other. The flies in a second group were instead given two identical copies of one of the other chromosomes (not the sex chromosomes), known as "autosomal chromosomes".

"There was no difference in average lifespan between females that had been inbred for the X chromosome and normal females. Inbreeding of one autosomal chromosome, on the other hand, did have a negative effect and the effects were equally large in females and males," says Martin Brengdahl.

The results suggest that having an unguarded X chromosome cannot explain the difference in lifespan between the sexes. At least, not in fruit flies.

"Genetic mechanisms are often relatively similar in different organisms, but we should be careful about drawing far-going conclusions from this study about how things work in humans. We have investigated the validity of the issue in one model, and further research can build on these results in the future," says Urban Friberg, senior lecturer at the Department of Physics, Chemistry and Biology, who has led the study.

The research group is now continuing to examine why there is a difference in lifespan between the sexes, and will be taking a close look at one of the alternative theories. In many species, competition between

males to mate with females is intense. The theory of sexual selection suggests that this may compel the males to use more energy in finding partners and less in maintaining bodily functions, which leads to a shorter lifespan.

**More information:** Martin Brengdahl et al. Sex differences in life span: Females homozygous for the X chromosome do not suffer the shorter life span predicted by the unguarded X hypothesis, *Evolution* (2018). DOI: 10.1111/evo.13434

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