XX protection against age-related mutations

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Protective effect of the second X chromosome in fruit flies. Credit: Asociación RUVID

Researchers at the University of Valencia's Cavanilles Institute of Biodiversity and Evolutionary Biology have put the 'unguarded X hypothesis' to the test and confirmed that differences in lifespan between the sexes, a widespread phenomenon in nature, may be due to the protective effect of having two copies of the X chromosome.

In this study, carried out in collaboration with the University of Oxford, researchers analysed the lifespans of male and female fruit flies (Drosophila melanogaster), having subjected both to different levels of inbreeding. The work, published in the journal *Biology Letters*, brings some much-needed empirical evidence in support of the 'unguarded X hypothesis', proposed 30 years ago to explain why XY males age faster

than XX females. Specifically, the study targets one of its fundamental predictions: that inbreeding shortens lifespan more in females than in males.

Pau Carazo, director of the research team at the UV, explains: "The differences in lifespan between the sexes can be partly explained by the fact that the accumulation of mutations over the course of a lifetime, or passed on from generation to generation, has a larger affect on the sex that has just one 'unguarded' copy of the X chromosome; generally males, including in human beings."

He adds, "If the guard effect is important, we can expect inbreeding to affect the lifespan of the homogametic sex (individuals with two of the same sex-determining chromosomes) to a greater extent than the heterogametic sex (with two different sex-determining chromosomes). This is because, in the latter group, the X chromosome is always 'unguarded', with or without inbreeding, while in the former group, the X chromosome is only 'guarded' if the two X chromosomes are different, which is not the case after repeated inbreeding."

The findings were consistent with this prediction.

The explanation for this 'guard' effect lies in the fact that most genetic mutations are by nature recessive. For XX individuals, this means they are only harmful when the same mutation occurs in both copies of the X chromosome; otherwise, they are simply not expressed. However, in the case of XY individuals, with no 'guard', any recessive mutation present in either the X or the Y chromosome would be expressed unconditionally. So by making the two X chromosomes in female fruit flies the same through inbreeding, the researchers essentially canceled out the protective effect of the second X chromosome, meaning that recessive mutations were expressed at the same rate among males as among females.

More information: Pau Carazo et al. Inbreeding removes sex differences in lifespan in a population of, *Biology Letters* (2016). DOI: 10.1098/rsbl.2016.0337

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