Researchers gain insight into chromosome evolution in flies

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Female Australian blowfly (Lucilia cuprina). Credit: Matt Bertone

NC State University researchers have shed new light on the evolution of fly chromosomes by identifying a gene indispensable for male survival in a devastating livestock pest species. What they found could have important implications for genetic pest control.

In a paper published June 7 in the journal *Current Biology*, entomologist

Max Scott and his colleagues outline findings of a recent DNA sequencing and bioinformatics study of the Australian sheep blowfly's X chromosome. The study supports an earlier hypothesis that the fourth chromosome of the much-studied fruit fly Drosophila melanogaster is derived from an ancient sex-determining X chromosome.

Scott's team found that of 59 genes on the X chromosome of the blowfly Lucilia cuprina, 49 mirror those in the fruit fly's fourth chromosome. The researchers also discovered that most of these genes are modulated by a dosage compensation mechanism, which equalizes gene expression between males and females of a species.

Males have only one X chromosome, while females have two. Different animals have different means of dealing with that genetic imbalance. In human females, for example, one of the X chromosomes is inactivated in all cells. But in Drosophila, nearly every gene on the male's X chromosome has an RNA output twice that of its female counterpart.

Because scientists know that a RNA-binding protein known as "painting of fourth," or POF, is key to regulating gene expression in Drosophila's fourth chromosome, Scott and his team thought a POF-like protein might be needed for normal levels of activity of genes on the X chromosome in Lucilia.

When the researchers used the CRISPR/Cas9 gene editing system to knock out the POF-related gene in Lucilia, they found that males died before they reached adulthood. In a nod to Scott's Australian heritage, the researchers call the gene "no blokes," or NBL. Females with the knocked-out NBL gene were fully viable and fertile.

The male mutants likely didn't live past the pupal stage because they could no longer double the output of X-linked genes, Max said.

"We think this is part of an ancient chromosome dosage compensation system in flies," Scott said. "We can't say for sure, but that's one interpretation of our data. Another interpretation of our data is that NBL is not involved in dosage compensation, but it is required for normal gene expression in the X chromosome in both sexes. Because they have only one X, males are more sensitive to the loss of NBL."

The study not only adds to the understanding of chromosome evolution, it could also inform research aimed at developing new genetic pest control systems.

Scott said that if further research confirms that the loss of NBL has little effect on female fitness, a Cas9-based gene drive targeting NBL in the female germline could be an effective way of controlling the Australian sheep blowfly as well as related livestock pests like the New World screwworm and possibly fruit flies such as the medfly. These pests cause millions of dollars of farm losses each year.

More information: Rebecca J. Davis et al. no blokes Is Essential for Male Viability and X Chromosome Gene Expression in the Australian Sheep Blowfly, *Current Biology* (2018). DOI: 10.1016/j.cub.2018.05.005

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