Ovulation shares both cellular and genetic features between fruit flies and mice

February 19 2015

Drosophila sp fly. Credit: Muhammad Mahdi Karim / Wikipedia. GNU Free Documentation License, Version 1.2

The average American woman lives more than 80 years and ovulates for 35 of them, producing an egg approximately once a month. The typical fruit fly lives about 4 weeks as an adult and ovulates every 30 minutes. Now researchers at the University of Connecticut report in *PLOS Genetics* that during a key process, the same gene may govern both. If correct, the results could bring insight to cancer metastasis, human fertility and ovarian disease.

We have a general idea of the timing of and the hormones involved in ovulation in humans. What we don't understand are the precise mechanics regulating how the egg escapes from the follicle of cells encasing it in the ovary. Does the egg shove its way out? Does the follicle bloom like a flower? What genes govern the process, and what do they do?

Researchers have tried to study the genetic mechanics of ovulation in designer 'knock-out' mice, which have one gene taken out of commission (or 'knocked-out'). But mice often have multiple, related genes in their genome and these genes can compensate for each other, so the process often still works even if a single gene is removed.

Fruit flies have a less-redundant genome and a faster life cycle than mice, making them much easier to work with. But researchers had assumed that insects are so far apart from us evolutionarily that their ovulatory process would be totally different.

Not so, according to Jianjun Sun and colleagues in UConn's department of physiology and neurobiology and their collaborator Allan Spradling at the Carnegie Institution for Science. In the February 19 issue of *PLOS Genetics* they report two critical parts of ovulation that seem to be the same in both flies and mice. The first is cellular, and has to do with the fate of the follicle cells after the egg escapes. Sun's team found that just as in mammals, in flies the follicle cells blocking the path of the egg out of the ovary degrade and slough off at ovulation. And just as in mammals, the follicle cells left behind inside the ovary after the egg escapes turn yellowish and produce steroid hormones essential for fertility.

The second has to do with Matrix metalloproteinase (Mmp), an enzyme that researchers suspect mammals need to break down the cellular matrix of the follicle in order for the egg to escape. Mice have 24 genes that code for Mmp: fruit flies have just two, mmp1 and mmp2. Sun and his colleagues found that knocking out just mmp2 all by itself reduced the mmps enzyme levels in a fly's ovaries, and dramatically reduced the number of eggs laid. This work provide the first genetic evidence that Mmp is required for ovulation and its role is likely conserved between flies and mice.

These similarities suggest that the basics of ovulation are very similar in animals generally.

"The evolutionary distance between flies and mice is so huge, compared to the distance between mouse and human. Everything that is conserved between fly and mouse is likely be conserved in humans," Sun says. The findings provide a foundation for other researchers to find out exactly which genes are required for ovulation in flies, and so for mice, and so for humans.

The research could prove immediately applicable to fertility disorders in humans such as polycystic ovary syndrome (PCOS), in which women don't ovulate. Sun's group is utilizing its fly system to look at PCOS now. But their findings could also prove useful to understanding the way cancer spreads through the body. When cancers metastasize, individual cells escape from the tumor mass and spread into the bloodstream. How exactly cancer cells escape from their original cell matrix may have something to do with the Mmp enzyme, Sun says, and that means this research could eventually inform treatments that block a cancer's spread.

Provided by University of Connecticut