

If a drug stops ovulation in both flies and mice, it's likely to work in humans, too

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When it comes to making eggs, female flies and female humans are surprisingly similar. And that could be a boon for women seeking better birth control methods, a UConn researcher reports in the July 5 issue of *PNAS*.

There are about 61 million women of reproductive age in the US, and about 43 millions of them are sexually active but don't want a pregnancy right now, according to the Guttmacher Institute. And while there are a



dozen or so different methods of <u>birth</u> control available, and most have undesirable side effects for some of the women who try them. Despite the need, pharmaceutical companies are not investing in new birth control research. Private funders such as the Bill and Melinda Gates Foundation have stepped up to fill the gap, and their efforts are bearing fruit in the lab of UConn physiologist and geneticist Jianjun Sun, an associate professor in the Department of Physiology and Neurobiology.

Sun and his colleagues have shown that compounds that stop <u>fruit flies</u> from ovulation (the process of releasing a viable egg) also prevent mice from doing so. And if a drug stops ovulation in both flies and mice, it's likely to work in humans, too. And that could make it much easier to screen potential birth control drugs quickly and effectively.

Several years ago, Sun's lab figured out how fruit flies ovulate. In a fly, as in a mouse or a human, many potential eggs mature inside the ovary. But to be fertilized, the eggs need to break out of the little cocoons, called follicles, they've been developing inside. Not all the eggs do this successfully; in humans it's usually just one per cycle. Sun's lab figured out exactly how successful eggs break out. Then he had a thought: now that we know how they break out, might it be possible to stop them? Stopping the egg from breaking out of the follicle would be a brand new form of birth control.

He applied for the Gates Foundation's Grand Challenges Explorations Award for birth control research, and won \$100,000 in 2016 for a proof of principle experiment: could fruit flies really be used to screen potential birth control drugs?

The answer, Sun found, is yes. He and collaborators at UConn Pharmacy, Northwestern University, University of Rutgers, and Michigan State University put fruit fly follicles in a dish and tested compounds from FDA's drug library. If the drug inhibited the fruit fly



eggs from ovulating, they then tested it on mice follicles. Of the 1,170 drugs they tried, six worked in flies. When they tested four of those in mice, three of them worked! And two seemed to work without affecting hormone levels. And one of those two drugs, chlorpromazine, is classified as a presumed human reproductive toxicant by the Netherlands due to its potential damage to human fertility; all the work so far has involved animal models.

Chlorpromazine, usually used to treat schizophrenia, is not a good candidate for birth control because of its psychoactive effects. But it does prove the concept: fruit fly ovaries can be used effectively to screen compounds for non-hormonal birth control.

More information: Kewa Jiang el al., "A platform utilizing Drosophila ovulation for nonhormonal contraceptive screening," *PNAS* (2021). www.pnas.org/cgi/doi/10.1073/pnas.2026403118

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