

## Reproductive tract secretions elicit ovulation

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Eggs take a long time to produce in the ovary, and thus are one of a body's precious resources. It has been theorized that the body has mechanisms to help the ovary ensure that ovulated eggs enter the reproductive tract at the right time in order to maximize the chance of successful fertilization.

New research from Carnegie's Allan Spradling and Jianjun Sun has shed light on how successful ovulation and fertilization are brought about by studying these processes in <u>fruit flies</u>. They found that secretions from special glands within the fruit fly's <u>reproductive tract</u> contribute to both ovulation and sperm function, and that this <u>secretion</u> is controlled by a specific <u>hormone receptor</u> gene, called Hr39. Their results suggest that Lrh-1, a mammalian receptor gene closely related to Hr39, also regulates ovulation by controlling reproductive tract secretions in mammals. Their findings are published by *eLife*.

Sun and Spradling's research provides an example of how the <u>biological</u> <u>processes</u> underlying a specific type of <u>human tissue</u> are often fundamentally similar to the biology of analogous tissues in seemingly very different species, such as insects. These common processes are not an accident, but rather are a consequence of the common <u>evolutionary</u> <u>history</u> of virtually all <u>multicellular organisms</u> on Earth. As a result of these similarities, researchers can genetically manipulate fruit flies in order to identify the genes and pathways controlling a biological process—in this case ovulation—and then use genome sequencing to identify the corresponding genes in other species, including humans.



Sun and Spradling began such a strategy a few years ago by characterizing how the glands within the ovary develop. Soon, they were able to tweak normal development to generate flies with anywhere from zero to the normal number of about 200 secretory cells, as well as adults in which secretory cell function could be turned on or off at will. Mice with the same properties would be a much bigger challenge to produce and would yield results much more slowly. Of course, such studies could not be undertaken with humans.

Using these special tools, the researchers confirmed that one important role of reproductive tract secretions is to protect and store sperm. At least 25 secretory cells are required, and their products attract sperm to glands where they can remain safely while bathed in the secretory fluid. Similar storage takes place in a region of the human Fallopian tube known as the isthmus. Sperm are thought to persist in the isthmus for only a few days, but can be stored for a week or more in the case of fruit flies. When production of the secretion is compromised, sperm have difficulty getting to the gland and those that can make it undergo abnormal changes.

The secretory "machinery" studied in these experiments may allow the reproductive tract to signal the <u>ovary</u> when it is ready to receive an egg. Waiting for such a signal before releasing an egg could reduce the chance that an egg would fail to enter the reproductive tract or arrive before active sperm were available.

Interestingly, Spradling and Sun's work shows that different secretions are responsible for ovulation from those responsible for attracting and storing sperm. Identifying the specific secretory cell products (and the corresponding genes) that are required for successful ovulation would be an important step in understanding the mechanisms of this still-mysterious process.



This research has a possible connection to one of the most common forms of ovarian cancer, which was recently shown to derive from abnormalities in reproductive tract <u>secretory cells</u>. The genes and pathways that cells use in carrying out their normal functions are often the targets of the alternations that drive cancer cell growth. Thus, this work should stimulate investigation of the role played by genes such as Lrh1 in this devastating disease.

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