More than just X and Y: A new genetic basis for sex determination

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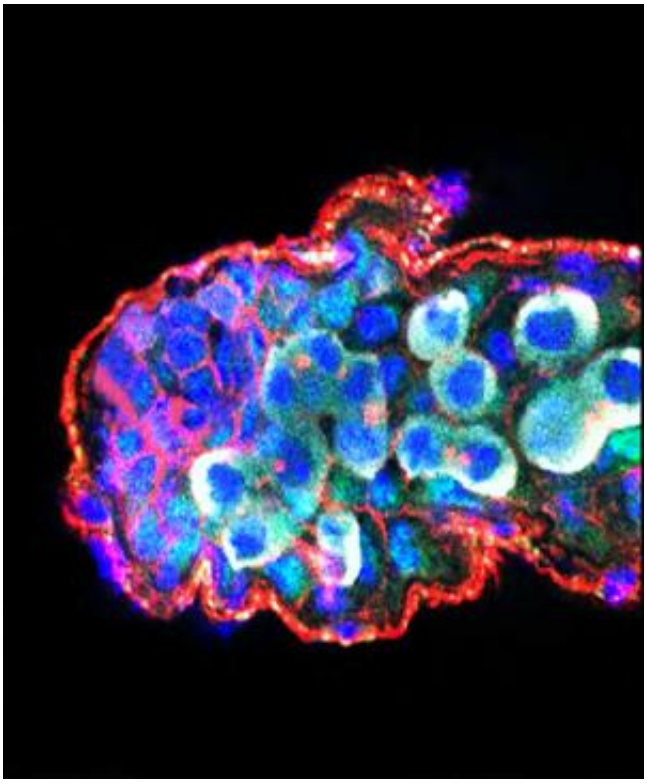

Cold Spring Harbor Laboratory researchers have found that miRNAs, short RNA molecules, are responsible for sexual differences in fruit flies. Shown here are testes from a male fruit fly where a hormone that controls a key miRNA has been inactivated. The abnormal testes fail to make sperm. They now produce sex determinants (shown in red) that are found in the ovaries of female flies. Credit: D. Fagegaltier/ Cold Spring Harbor Laboratory

Men and women differ in plenty of obvious ways, and scientists have

long known that genetic differences buried deep within our DNA underlie these distinctions. In the past, most research has focused on understanding how the genes that encode proteins act as sex determinants. But Cold Spring Harbor Laboratory (CSHL) scientists have found that a subset of very small genes encoding short RNA molecules, called microRNAs (miRNAs), also play a key role in differentiating male and female tissues in the fruit fly.

A miRNA is a short segment of RNA that fine-tunes the activation of one or several protein-coding genes. miRNAs are able to silence the genes they target and, in doing so, orchestrate complex genetic programs that are the basis of development.

In work published in *Genetics*, a team of CSHL researchers and colleagues describe how miRNAs contribute to sexual differences in fruit flies. You've probably never noticed, but male and female flies differ visibly, just like other animals. For example, females are 25% larger than males with lighter pigmentation and more abdominal segments.

The team of researchers, including Delphine Fagegaltier, PhD, lead author on the study, and CSHL Professor and Howard Hughes Medical Institute Investigator Greg Hannon, identified distinct miRNA populations in male and female flies. "We found that the differences in miRNAs are important in shaping the structures that distinguish the two sexes," says Fagegaltier. "In fact, miRNAs regulate the very proteins that act as sex determinants during development."

The team found that miRNAs are essential for sex determination even after an animal has grown to adulthood. "They send signals that allow germ cells, i.e., eggs and sperm, to develop, ensuring fertility," Fagegaltier explains. "Removing one miRNA from mature, adult flies causes infertility." More than that, these flies begin to produce both male

and female sex-determinants. "In a sense, once they have lost this miRNA, the flies become male and female at the same time," according to Fagegaltier. "It is amazing that the very smallest genes can have such a big effect on sexual identity."

Some miRNAs examined in the study, such as let-7, have been preserved by evolution because of their utility; humans and many other animals carry versions of them. "This is probably just the tip of the iceberg," says Fagegaltier. "There are likely many more miRNAs regulating sexual identity at the cellular and tissue level, but we still have a lot to learn about these differences in humans, and how they could contribute to developmental defects and disease."

More information: "A Genome-Wide Survey of Sexually Dimorphic Expression of Drosophila miRNAs Identifies the Steroid Hormone-Induced miRNA let-7 as a Regulator of Sexual Identity" appeared online in *Genetics* on July 31, 2014.

Provided by Cold Spring Harbor Laboratory

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