Male or female? In flies, some cells can't tell

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fruit fly

An experienced fruit fly researcher can tell at a glance whether the fly she is observing is male or female; a distinct pigmentation pattern on a fly's body (a type of bristle found only on the legs of males) and differences in the genitalia are dead giveaways. But most of the fly's body parts look identical in males and females, and until now, scientists had no idea whether "maleness" or "femaleness" extended to all of the insect's cells and tissues. In a study publishing today in the online, open access journal *PLoS Biology*, researchers at the Janelia Farm Research Campus of the Howard Hughes Medical Institute find that most cells in flies' bodies are identical, regardless of whether they are in a male or a female.

This is because the influence of sex-determining genes is restricted to specific tissues, says Bruce Baker, a group leader who conducted the research with colleagues Carmen Robinett, Alex Vaughan, and Jon

Michael Knapp. Baker has been studying the genetics of fruit fly sex for 30 years. By the early 1980s, it was known that a cascade of genes determines how tissues and organs develop in a sex-specific manner. In this bureaucratic chain of command, each gene tells the next one how and when to act.

The doublesex gene, the master gene that determines sexual characteristics, is the last gene in the cascade. In flies, females express one form of doublesex, and males another. This gene is viewed as a master switch that tells female cells to create female sexual characteristics and male cells to make male ones. Until now, fly geneticists clung to the notion that the male version of doublesex was switched on in every cell of male flies, while the female version was present in every cell in female flies.

Prompted by other labs reporting that doublesex is turned on only in small areas in the fly embryo and only in specific parts of the brain, Robinett and her colleagues employed a genetic engineering technique to detect doublesex expression in the cells of developing flies. The technique attaches a reporter gene to doublesex that makes cells expressing the gene glow green. Tracking doublesex then becomes as easy as watching for green spots in fly embryos, larvae, and adults. With this approach, Baker's group found that during fly development, doublesex switches on and off at different times and in different tissues. As expected, they saw doublesex protein in the genitalia and in other body parts that display differences between males and females. But in body parts where there are not overt differences between males and females, they found that doublesex was expressed only in certain cells and not expressed in many other types of cells.

"It's a simple observational study with profound implications," Baker says. This study demonstrates that only a subset of cells is likely to know whether they are male or female. Robinett and her colleagues found that

male and female fruit flies are really a mixture of cells that are sex-specific and cells that are sexless. Many of the fly's cells never turn on the doublesex gene. So while, some cells "know" their sex and take on sex-appropriate characteristics during development, those that do not express doublesex remain identical in males and females.

Because doublesex or analogous genes are present in myriad organisms, including humans, this theme may apply to more than fruit flies. "It may be broadly true that males and females are made up of a mosaic of cells that know their sex and cells that don't," Baker says. This could prompt other researchers to check for similar doublesex patterns in other model organisms such as roundworms, zebrafish, and mice. If similar findings emerge, it could shake up the entire notion of sex differences in the animal kingdom. And if the finding applies to humans - a big "if" at this point - the implications could be even more significant. "If it applies to people, it's certainly going to change our sociological view of what we think of as maleness and femaleness."

More information: Robinett CC, Vaughan AG, Knapp J-M, Baker BS (2010) Sex and the Single Cell. II. There Is a Time and Place for Sex. PLoS Biol 8(5): e1000365. doi:10.1371/journal.pbio.1000365

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