

## SEX DETERMINATION

## The means to discriminate

Nature has a startling number of ways in which to establish differences between the sexes, and now a couple more can be added. In melons, an integrated model of sex determination — based on epigenetic repression mediated by a transposon — has been proposed to explain the development of male, female and hermaphrodite flowers, and in honeybees, it has been shown that sexual differentiation is a two-step process.

Sex determination in plants involves the physical separation of male and female flowers either on the same plant or in different individuals. In melons, the differentiation of the different sexual forms is controlled by a two-locus system, but the underlying mechanism remains unclear. To investigate this problem, Martin *et al.* positionally cloned the locus responsible for the transition from male to female flowers by crossing a

monoecious plant (which contains both male and female flowers) with a gynoecious plant (in which all flowers are female). This led them to identify a *hobo*, *Ac*, *Tam3* (hAT) family transposon insertion that, in all gynoecious lines tested, causes DNA hypermethylation at the promoter of the *WIP1* gene. *WIP1* encodes a zinc-finger transcription factor that blocks the development of the female reproductive organs. Hypermethylation of this gene in gynoecious lines silences *WIP1* expression and therefore permits the appearance of female flowers. Furthermore, repression of *WIP1* indirectly leads to the activation of another gene, *ACS7*, which arrests the development of male reproductive organs. The relative activity of *WIP1* and *ACS7* can therefore explain the formation of male, female and hermaphrodite flowers — in this last case, male reproductive organs are produced because of *WIP1* repression and the presence of a non-functional *ACS7* gene.

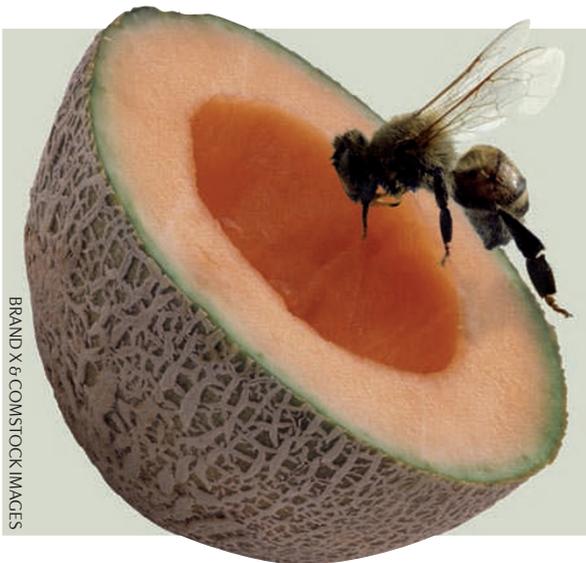
Honeybees have an unusual sex determination system whereby females develop from embryos that are heterozygous for alleles at the sex determination locus (SDL), whereas males develop when the locus is either homozygous or (in the case of unfertilized eggs) hemizygous. The SDL contains five protein-coding genes, but Gempe *et al.* established that only two — *complementary sex determiner* (*csd*) and its paralogue *feminizer* (*fem*) — function in sex determination. The authors characterized these genes by small interfering RNA (siRNA) injection into embryos. The *csd* gene

is the primary determinant of sex, but how is it linked to downstream sexual differentiation? Both *csd* and *fem* are required for female differentiation, because in *csd*- and *fem*-repressed females both the soma and germ line are switched to the male fate. Removal of *csd* or *fem* activity by siRNA causes male-specific splicing of *fem* and the downstream *doublesex* gene. This result implies that male is the default sex-differentiation pathway. However, a striking finding was that *csd* can only support female-specific splicing of *fem* early in development; at later larval stages, female-specific *fem* activity is maintained by positive feedback of the Fem protein on the splicing of its mRNA. So, although *csd* provides a primary read-out of the allelic status at the SDL, *fem* is needed to maintain the female mode of development.

Although these mechanisms may seem peculiar to these two species, the involvement of an epiallele in determining sex points to the adaptability of this trait in melons, whereas the two-tier differentiation system in honeybees allows mechanistic comparisons of orthologous genes across 270 million years of insect evolution.

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**ORIGINAL RESEARCH PAPERS** Martin, A. *et al.* A transposon-induced epigenetic change leads to sex determination in melon. *Nature* **461**, 1135–1138 (2009) | Gempe, T. *et al.* Sex determination in honeybees: two separate mechanisms induce and maintain the female pathway. *PLoS Biol.* **7**, e1000222 (2009)  
**FURTHER READING** Williams, T. M. & Carroll, S. B. Genetic and molecular insights into the development and evolution of sexual dimorphism. *Nature Rev. Genet.* **10**, 797–804 (2009)



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