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## EVOLUTION:

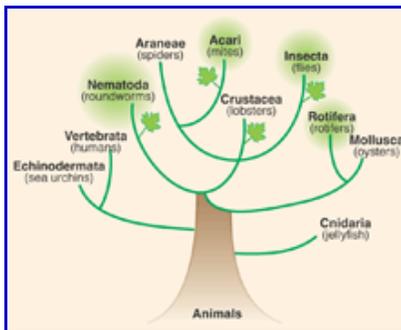
### Haploids--Hapless or Happening?

Sarah P. Otto and Philippe Jarne\*

In biology, it seems, there are exceptions to every rule, although sometimes finding these exceptions can be exceedingly difficult. Typically, animal cells are diploid, that is, they carry two copies of each chromosome, except during a brief phase when haploid gametes (sperm and egg) with half the normal chromosome complement are produced. Although haplodiploidy (haploid males and diploid females) has arisen many times during evolution, so far no animal has been found to exist exclusively in the haploid state (1). Enter the false spider mite *Brevipalpus phoenicis* on page 2479 of this issue, a daring exception to the rule that diploidy dominates (2). The discovery by Weeks *et al.* (2) that *B. phoenicis* exists only in the haploid state calls into question the dogma that diploidy has been selected for during animal evolution because of the fitness benefits it confers.

The false spider mite and its relatives *B. obovatus* and *B. californicus* reproduce by parthenogenesis, that is, females produce only female offspring from unfertilized eggs. The eggs and adult cells of these female mites contain two chromosomes, but it has been difficult to decipher whether the two chromosomes are unrelated, indicating a haploid state, or duplicates of each other (homologs), indicating diploidy. Weeks *et al.* prove that these two chromosomes are genetically distinct and conclude that the female mites are haploid. They found that only one of the two chromosomes contains a nucleolar organizing region, and only one carries an 18S ribosomal DNA gene (if the two chromosomes are homologs, they would carry copies of the same genes in the same locations). Furthermore, even though the investigators surveyed 45 clonal lines of *B. phoenicis* at seven highly polymorphic microsatellite loci, they were unable to find any individuals that carried more than one copy (allele) of a particular gene, indicating that these mites are indeed haploid.

How did these haploid oddities arise? Weeks *et al.* noticed that the eggs of *B. phoenicis* were laden with intracellular bacteria. Treatment with antibiotics led to loss of bacteria in roughly half the eggs. The infected offspring continued to develop as females, as expected, but the cured offspring developed into males! This observation is not as bizarre as it seems. Closely related mites (*B. russulus*) are haplodiploid yet reproduce sexually, indicating that haploid males must have been present among the ancestors of this group. Weeks *et al.* suggest that infection of a sexual haplodiploid ancestor with "feminizing" intracellular bacteria caused haploid eggs that normally developed as males to develop into females. The obvious culprit to suspect is the infamous intracellular bacterium *Wolbachia* (phylum Proteobacteria), which infects a variety of insect species, feminizing the males or killing them off (see the figure) (3). In the case of the false spider mite, however, *Wolbachia* is innocent. In fact, as Weeks *et al.* report, the bacterium infecting *B. phoenicis* is not even closely related to *Wolbachia*, but belongs to a different phylum (Cytophaga-Flavobacterium-Bacteroides) altogether.



**The mighty mite.** The false spider mite, *B. phoenicis*, is the first animal known to exist solely in the haploid state. In contrast, haplodiploidy (male haploids, female diploids) has arisen at least 17 times during animal evolution (groups highlighted in green). Intracellular bacteria that affect sexual development (especially *Wolbachia*) have been found in many of these haplodiploid groups (indicated by a leaf). The tree shape (but not branch lengths) is based on a molecular phylogeny of the animal kingdom (14). Examples of the different animal groups are given in parentheses. [The distribution of haplodiploidy and *Wolbachia* in the animal kingdom is presented in (15).]

SOURCE: A.WEEKS

Feminizing bacteria could have spread rapidly through the ancestral population of *B. phoenicis*. Because the bacteria cause all offspring of infected mites to develop into females, infected mites do not have to divide energy resources between sons and daughters. Thus, feminizing bacteria have enabled *B. phoenicis* to avoid the costs of sexual reproduction (4). Whether meiosis (cell division in which the chromosome complement is halved) is suppressed immediately in newly infected haploid females is still not known. If meiosis continues after infection, the lack of homologous chromosomes would result in aberrant chromosome segregation during cell division. Also unclear is whether infected female mites can reproduce sexually with haploid males that may arise intermittently. Haploid males must have existed during the initial spread of the bacterial infection and have been found in some field populations (5). Furthermore, in the laboratory, males can be readily produced by cultivating the mites at high temperatures or by treating them with antibiotics (2). Rare matings between infected females and cured males would dramatically increase genetic variability within an otherwise clonal population, especially if the resulting diploids are infected and produce haploid daughters without fertilization. In short, these haploid mites avoid the costs of sexual reproduction although they may occasionally indulge in sex, thus gleaning many of its benefits.

Why has it taken so long to uncover a case of haploidy among female animals? Given that haplodiploidy (haploid males, diploid females) has arisen repeatedly, one might expect to see animals with reverse haplodiploidy (haploid females, diploid males). Yet reverse haplodiploidy has never been observed, perhaps because it poses

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several evolutionary dilemmas (6). If haploid daughters were to inherit their father's genome, there would be strong selection on mothers to avoid producing such daughters, which lack the maternal genome. On the other hand, if haploid daughters were to inherit their mother's haploid genome, the female lineage would be entirely devoid of genetic recombination, giving rise to problems concomitant with asexuality (such as the loss of genetic variability). Furthermore, although the standard form of haplodiploidy enables an unfertilized diploid female to colonize new habitats and to produce sons with whom she can mate, reverse haplodiploidy provides no such benefit. It is intriguing that this first example of a haploid female animal involves feminization of haploid males rather than a reversal of the usual form of haplodiploidy.

Counterexamples to supposedly general rules can be extremely useful, especially when they reveal a false premise upon which the rule is based. The fact that nearly all animals are diploid has been taken as evidence for the inherent superiority of the diploid state, arguably because the extra copy of each gene masks the deleterious effects of mutations. This argument is specious, however, because haploid development is common in almost every other group of organisms (7) and because masking mutations allows mutant alleles to accumulate over time so that diploid populations generally have a lower long-term fitness. An alternative possibility is that diploidy became a "frozen accident" early in the evolution of multicellular animals, after which reverting to the haploid state became problematic (8). One can imagine that mechanisms evolved that restricted mitosis (cell division in which the chromosome complement remains the same) to diploid cells. An example of such a mechanism in mammals is the requirement for a balance between maternally and paternally imprinted genes. The discovery of female haploid animals, along with the fact that haploid males have evolved repeatedly (see the figure), demonstrates that there is no process that absolutely prevents animals from developing as **haploids**.

Another reason why the diploid state may have become "frozen" within animal groups is that **haploids**, when they arise, may perish immediately from the full impact of deleterious recessive alleles, which are masked but reach appreciable frequencies in diploid populations (9). In humans, for example, the frequency of these nefarious alleles is so high that any haploid offspring would carry twice the lethal load of these alleles and would die before reaching maturity (10); fortunately, unaffected copies of mutated genes allow us to survive. Plants express 60 to 70% of their genes during the haploid gamete-producing stage (11)—the expression of so many genes acts as a sieve, limiting the accumulation of recessive deleterious alleles. In animals, however, this sieve is thought to be virtually absent. Gene expression during the haploid gametic phase decreased dramatically in our protist ancestors when they evolved a compact sperm nucleus (12). Later, there was a further drop in haploid gene expression with the evolution of a metabolically quiescent egg, which subsists on gene transcripts produced primarily during an early diploid stage (prophase I) of meiosis. But some gene expression in the haploid state of animals does remain, even among vertebrates (13), albeit with considerable variability.

We need to compare gene expression patterns in the haploid and diploid states as well as mutation rates among mites and other animal lineages that have given rise to haploid individuals. In this way, we may discover why haploidy has arisen in some, but not other, groups of predominantly diploid organisms.

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S. P. Otto is in the Department of Zoology, University of British Columbia, Vancouver V6T 1Z4, Canada. P. Jarne is at CEFE-CNRS, 34293 Montpellier Cedex 05, France. E-mail: [otto@zoology.ubc.ca](mailto:otto@zoology.ubc.ca)

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