



# When it comes to genetics, cheaters do prosper

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Received: 15 June 2022 / Revised: 16 June 2022 / Accepted: 16 June 2022  
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From a genetic element's point of view, sexual reproduction is a life-or-death situation. Should it have the luck of being passed on to progeny, then the genetic element will live on in the next generation. If it is not fortunate enough to be inherited, however, then the legacy of that genetic element is dead. This process is random, meaning that there is an equal chance that a genetic element will or will not be inherited. We refer to this inheritance pattern as being Mendelian because it follows the rules described by Gregor Mendel in his seminal experiments with pea plants. After crossing together distinct varieties to create hybrids (and then crossing these hybrids to one another), Mendel meticulously recorded the inheritance patterns of dominant and recessive characteristics (Mendel 1865). His 8-year experiment yielded three laws that have held true and grown to become the cornerstone of classic genetics: the Law of Dominance, the Law of Segregation, and the Law of Independent Assortment.

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Responsible Editor: Rachel O'Neill

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Though most genetic elements abide by these laws, others routinely break them to increase their chances of being passed on to the next generation. This unlawful behavior by selfish genetic elements enables their maintenance in a population generation after generation, even if their presence is detrimental to the host (McLaughlin and Malik 2017; Ågren and Clark 2018; Zanders and Unckless 2019). It is difficult to comprehend how a genetic element would persist despite their harmful effects, but as Ostergren first pointed out, such elements need not be useful to their host, “they need only be useful to themselves” (Ostergren 1945). The concept that a detrimental genetic element could promote its own inheritance meant that such behavior could effectively short-circuit natural selection and be a potent evolutionary force. This observation was not lost on Sandler and Novitski, who introduced the term “meiotic drive” to describe the behavior of selfish genetic elements that exploit the meiotic divisions to drive their transmission and be inherited in ratios greater than those predicted by Mendelian inheritance (Sandler and Novitski 1957).

In recent years, the meiotic drive field has seen extensive growth fueled by the advancement of genetic and genomic technologies, with many mechanistic insights into drive and discoveries of new drive systems. As this Chromosome Research Special Issue on “Non-Mendelian Inheritance and Meiotic Drive” illustrates, these selfish genetic elements are as diverse as they are sophisticated. The ten articles and reviews

contained in this Special Issue showcase different drive systems that are found over a broad range of species.

Drive systems are roughly categorized as being either “true” or “killer” depending on their mechanism of action. To be transmitted at higher-than-Mendelian ratios, selfish genetic elements must either actively promote their inclusion in the final haploid product (true drive) or eliminate their competition so that they become overrepresented (killer drive) (Núñez et al. 2018). One type of killer drive system is the sex-ratio distorter, which causes a distortion in the ratio of males to females. To understand the evolutionary dynamics of a sex-ratio distorter, Bastide et al. focus on the X-linked Paris *sex-ratio* system from the fruit fly *Drosophila simulans* in an experimental evolution study and follow the maintenance of the driver over nearly 100 generations while under strong drive suppression. Though drive suppression in wild populations can lead to a decrease in driver frequency, Bastide et al. found that the driver in some replicates of their controlled population experiment was maintained, indicating that suppression of deleterious drivers may act to slow down their elimination from the population.

Another well-known killer drive system is the *t*-haplotype in the house mouse *Mus musculus* (Fraser and Dudley 1999). Males that are heterozygous for the *t*-haplotype (+/*t*) will almost exclusively pass on the *t*-haplotype to their progeny because the wild type (+) sperm have poor mobility and therefore rarely make it to the egg before *t*-bearing sperm. This poor mobility is caused by a gene product expressed from the *t*-haplotype, but, as shown by Winkler and Lindholm, the *t*-bearing sperm may not be entirely immune to their own poison. There appears to be lasting damage to the *t*-bearing sperm as well, leading Winkler and Lindholm to propose that this may be evidence of “spiteful” behavior. Indeed, *Mus musculus* can serve as a powerful model system for drive, which is expertly discussed by Arora and Dumont. In their review, Arora and Dumont touch on several known drive systems in house mice, present an overview of the resources that can be harnessed to identify new drive systems, and provide a prospective look at how advanced technologies and modern molecular tools can be applied to study selfish genetic elements in mammals.

True drive systems do not actively antagonize their competition; instead, they typically exploit an inherent asymmetry that enables them to be inherited at a higher-than-Mendelian frequency. Dudka and

Lampson review a form of true drive termed “centromere drive” in two species, *Mus musculus* and the monkeyflower *Mimulus guttatus*. Centromeres attach to spindle microtubules to coordinate chromosome segregation. If a centromere was to turn selfish, it may bias its segregation during asymmetric cell divisions (like female meiosis) to increase its transmission frequency. In their review, Dudka and Lampson discuss conceptual and mechanistic details behind centromere drive and outline the future directions of the centromere drive field.

A classic true drive system involves the abnormal chromosome 10 (Ab10) in maize (*Zea mays*). This chromosome has “knobs” at one of its ends composed of heterochromatin that act as neocentromeres and can direct the segregation of the Ab10 during female meiosis and increase its transmission frequency. Dawe elegantly describes the history of Ab10 and its knobs from their discovery and early characterization in the 1930s using genetics and cytogenetics, the segregation of Ab10 and its ability to drive during female meiosis, and the mechanism of its drive using kinases that are located proximal to the knobs.

Though the term “meiotic drive” was originally meant to be reserved for selfish genetic elements whose mechanism was known to occur during the meiotic divisions, it has been used as a catch-all term to describe selfish behavior regardless of when it occurs during sexual reproduction. To help clarify the terminology, Camacho breaks down eight steps during the reproductive cycle that provide opportunities for selfish genetic elements to distort their transmission ratio. Camacho provides examples of transmission ratio distortion at each of these steps for a specific type of selfish genetic element: the B chromosome. B chromosomes are supernumerary, non-essential chromosomes, and though their presence can be detrimental to the host, many B chromosomes have developed complex mechanisms that enable them to be inherited at high frequencies.

Many B chromosomes carried by plants exhibit non-Mendelian inheritance, but two of the most well-studied examples are the B chromosomes in maize (*Zea mays*) and rye (*Secale cereale*). These B chromosomes use sophisticated mechanisms to ensure they are transmitted at greater-than-Mendelian frequencies to the next generation. In their review, Chen, Birchler, and Houben masterfully describe B chromosome behavior in several plant species and pay particular attention to the intricacies of how the B

chromosomes in maize and rye bias their segregation during the post-meiotic pollen mitoses.

Accessory chromosomes found in fungi like *Zyoseptoria tritici* are similar to B chromosomes in that they are non-essential and have been shown to exhibit non-Mendelian transmission. Komluski, Stukenbrock, and Habig examine the accessory chromosomes across different fungal eukaryotes and discuss the processes and structural traits that allow them to bias their segregation during sexual reproduction, providing a strong case as to how the versatility of accessory chromosomes in fungi can add to our understanding of factors that promote non-Mendelian inheritance of entire chromosomes.

The germline-restricted chromosome in songbirds is an interesting example of a chromosome that displays non-Mendelian inheritance and, as its name implies, is only carried in the germline and not in the somatic tissue. Germline-restricted chromosomes were first found in the zebra finch *Taeniopygia guttata*, but as Borodin et al. detail in their review, they have since been found in all songbirds that have been cytologically examined. These “Mendelian nightmares” undergo programmed elimination in the somatic tissue and in male germ cells before the end of meiosis, making them intriguing models for understanding non-Mendelian behavior of chromosomes.

Another model for unusual chromosome mechanics is *Bradysia* (previously called *Sciara*). In Gerbi’s review, the dynamics of chromosome elimination and biased segregation in somatic and germline tissue are thoroughly discussed. Similar to the germline-restricted chromosome in songbirds, the L chromosome of the fly *Bradysia* (*Sciara*) is also limited to the germline due to its elimination in somatic tissue. Gerbi also describes how chromosome segregation during male meiosis in *Bradysia* (*Sciara*) is non-random: the paternal chromosomes are segregated from the maternal chromosomes at the first meiotic division and are discarded, providing the first example of imprinting. Clearly, this tiny fly has a lot to teach us about non-Mendelian inheritance.

This Chromosome Research Special Issue on “Non-Mendelian Inheritance and Meiotic Drive” provides an excellent cross-section of the field. Without the invaluable contributions from our colleagues, this Special Issue would not have been possible. Therefore, we would like to extend our gratitude and appreciation to each of the authors who gave their time to craft a contribution to this Special Issue, as well as the expert reviewers who provided valuable feedback to our authors. It was our pleasure to bring together the ideas and perspectives from such a wide variety of systems. We are also indebted to both the Editor-in-Chief Dr. Beth A. Sullivan and Executive Editor Dr. Rachel O’Neill for their guidance and expertise during the assembly of this Special Issue.

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