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REVIEW

The maize abnormal chromosome 10 meiotic drive haplotype: a review

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Abstract The maize abnormal chromosome 10 (Ab10) haplotype encodes a meiotic drive system that converts heterochromatic knobs into centromere-like bodies that are preferentially segregated through female meiosis. Ab10 was first described in the 1940s and has been intensively studied. Here I provide a comprehensive review of the literature, starting from the discovery of knobs and Ab10, preceding through the classic literature, and finishing with molecular structure and mechanisms. The defining features of the Ab10 haplotype are its two specialized kinesins, *Kinesin driver* and *TR-1 kinesin*, that activate neocentromeres at knobs containing different classes of the tandem repeat. In most Ab10 haplotypes, the two kinesin/knob systems cooperate to promote maximum meiotic drive. However, recent interpretations suggest that each kinesin/knob system can function as an independent meiotic driver and that in some cases they compete with each other. Ab10 is present at low frequencies throughout the genus *Zea* and has significantly expanded genome size by promoting the formation of knobs throughout the genome.

Keywords Maize · Meiotic drive · Ab10 · Knobs · Heterochromatin · Neocentromere · Kinesin · Kinesin-14 · Tandem repeat

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Introduction

Meiotic drive describes genes or structural elements of the genome that evade the constraints of Mendelian segregation and spread through populations without regard to organismal fitness (Sandler and Novitski 1957; Lindholm et al. 2016). Many well-known examples of meiotic drive do not involve changes to meiosis and instead affect post-meiotic processes such as sperm function (Presgraves 2009; Courret et al. 2019). Those that act at the level of meiosis generally affect female meiosis where only one daughter cell becomes the egg (Pardo-Manuel de Villena and Sapienza 2001). Falling into the latter category are examples of centromere drive, where larger centromeres are preferentially transmitted in some species, the preferential transmission of some B chromosomes, and the maize abnormal chromosome 10 haplotype (Ab10) (Rhoades and Others 1952; Lampson and Black 2017; Clark and Akera 2021). In this review, I focus entirely on Ab10, intending to provide a comprehensive summary of all that is known about the haplotype and its phenotypes. In addition to the

historic literature, I highlight recent results showing that Ab10 encodes two meiotic drive systems embedded within one another, both based on the activation of neocentromeres at heterochromatic knobs, but involving the actions of separate kinesins operating on distinct tandem repeats.

Discovery of knobs

Maize genetics is often thought of as beginning in a small group of young scientists at Cornell University, led by the wisened plant geneticist Rollins Emerson (Rhoades 1984). Among his proteges were Barbara McClintock and Marcus Rhoades, both of whom were superb cytogeneticists. McClintock was searching for cell types that made it possible to identify individual chromosomes and ultimately arrived at the pachytene substage of meiosis when homologous chromosomes are aligned along their lengths. She and others learned to identify the chromosomes based on size and arm ratio, as well as characteristic heterochromatic regions, the most prominent of which were large "knobs"—intensely staining condensed regions of chromatin in mid-arm locations (McClintock 1931). Over time, it became clear that knobs were found at as many as 34 predictable locations, but the presence or absence, and size of a knob at any given site varied among lines (Longley 1937, 1938; Kato 1976). Knobs are composed of two classes of tandem repeats—a ~ 180-bp repeat called knob180 (Peacock et al. 1981) and a ~ 360-bp repeat called TR-1 (Ananiev et al. 1998). Most knobs contain a mixture of knob180 and TR-1 repeats, with a small subset appearing to have only knob180 or TR-1 (Swentowsky et al. 2020; Hufford et al. 2021).

Discovery of Ab10

Abnormal chromosome 10 was discovered by a scientist working outside the Cornell sphere of influence, Albert Longley, in a small lab in Washington DC. He was the first to carry out surveys of different maize and teosinte lines based on chromosome cytology alone (Longley 1937, 1938). Having noted that chromosomes from different lines had similar overall structures, he was struck by the fact that there were two obviously different forms of chromosome 10. The Abnormal type (Ab. 10, later shortened to Ab10) had an additional piece on the end of the long arm that was approximately the size of the short arm. Depending on the line, the additional piece on Ab10 could have either one large knob (Ab10-I) or two adjacent large knobs (Ab10-II, see below). He naturally thought it might be a translocation of a part of one chromosome to the end of chromosome 10, but ultimately concluded that "Nothing in the character of the additional piece found attached to the tenth chromosome has suggested a solution of its origin" (Longley 1938).

Meiotic drive by Ab10

Marcus Rhoades was actively working on building out the maize genetic map and was interested in using the easily scorable cytological abnormality on Ab10 as a way to measure the distance between a gene called *Colored-1* (*R1*) and the end of the long arm of chromosome 10. *R1* is one of several color genes that are required to confer a purple color to the outer layers of cells of the maize kernel. Simple testcrosses revealed that the recessive *r1* allele linked to the extra segment on Ab10 was significantly overrepresented, transmitted to about 70% of the progeny instead of the expected 50% (Rhoades 1942). He then selected recombinants where *R1* was linked to the extra piece and again made testcrosses, and again observed ~ 70% transmission of *R1* and the extra segment. These effects were only observed through female crosses. When Ab10 was crossed as a heterozygote through the male it was at a slight disadvantage. He explored several potential explanations for this behavior, including selective abortion of embryos containing the normal chromosome, megaspore competition (where a cell other than the basal megaspore becomes the egg), and the possibility that gravity was pulling the knobs downward, and ruled them all out (Rhoades 1942). He concluded that something inherent to the extra segment on Ab10 was causing it to be preferentially segregated to the egg cell.

Longley then extended this line of study to look at the segregation of other knobs when Ab10 was present (Longley 1945). He identified morphological markers linked to knobs, paired them with chromosomes that lacked knobs, and testcrossed as females in the presence of Ab10. Genes linked to

knobs on chromosome 6 and 9 showed pronounced preferential segregation particularly for genes closest to knobs. Others demonstrated that genes linked to knobs on chromosome 3 and 4 showed the same behavior (Rhoades and Dempsey 1966; Dawe et al. 2018). These data led to the conclusion that Ab10 can cause the preferential segregation of any knob in the genome, provided it is heterozygous with a chromosome that lacks a knob.

Neocentromeres

In the same year that Rhoades described Ab10-mediated meiotic drive, he and his student described a remarkable cytological phenomenon in lines carrying Ab10 (Rhoades and Vilkomerson 1942). At both meiosis I and II, knobs in lines carrying Ab10 move rapidly to the poles, stretching chromosome arms in the process. He called knobs in their mobile form "neocentromeres" (not to be confused with the shifting of true centromeres to different chromosomal locations (Dawe and Hiatt 2004)). Live and fixed-cell microscopy demonstrated that neocentromeres move poleward 38% faster than true centromeres (Yu et al. 1997) and slide alongside bundles of microtubules instead of interacting with microtubules end-on like true centromere/kinetochores (Yu et al. 1997). The rapid sliding motion suggests that neocentromeres move by a mechanism unrelated to normal centromere movement. Consistent with this view, antisera against four maize kinetochore proteins (CENH3, CENP-C, MAD2, NDC80) failed to show any localization to active neocentromeres (Dawe et al. 1999; Dawe and Hiatt 2004). The poleward movement of heterochromatic regions has also been observed in several other plants (Dawe and Hiatt 2004), although only in maize have neocentromeres been causally associated with the meiotic drive.

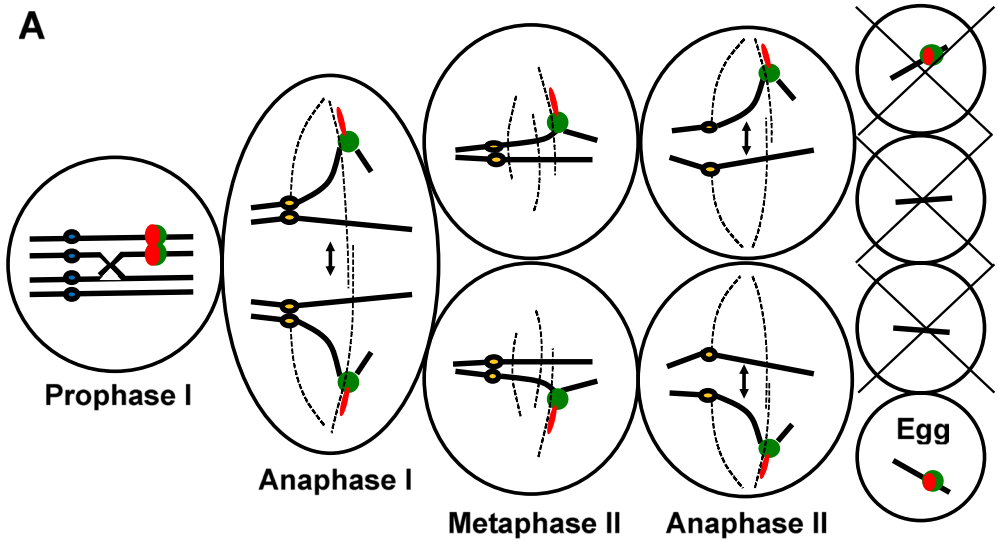
Role of recombination in meiotic drive

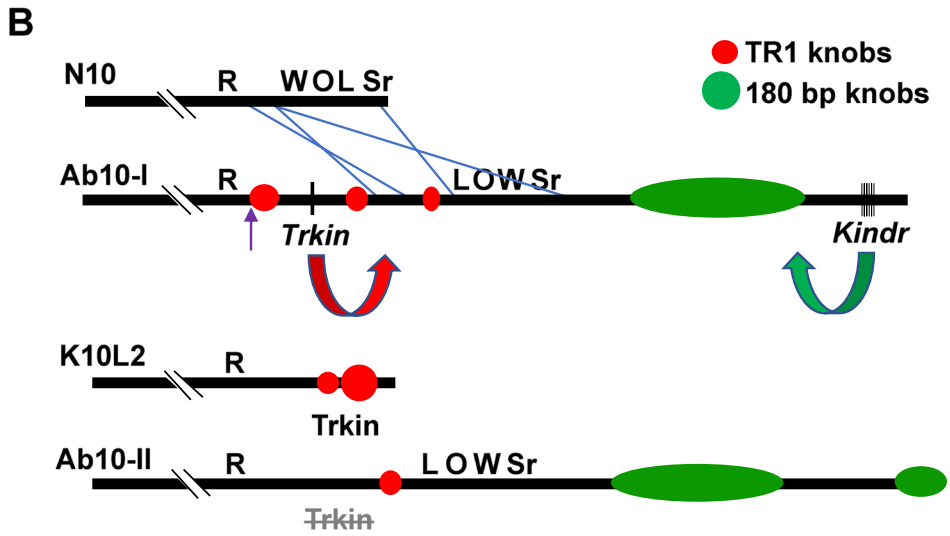
Knobs tend to be located far enough from centromeres that recombination between centromere and knob is very likely (Longley 1939). Rhoades suspected that recombination between centromeres and knobs may be required for the meiotic drive. He understood that a single recombination between centromere and knob would make each chromosome have one knobbed chromatid and one non-knobbed chromatid (Rhoades 1942). Once this occurred, all that was needed was a mechanism for the knobbed chromatid to be preferentially transmitted to the egg cell in meiosis II. He and his long-time research associate Ellen Dempsey proceeded to carry out detailed studies of recombination in Ab10 lines (Rhoades and Dempsey 1966). They concluded that meiotic drive occurs after a crossover in the centromere-knob interval and is not affected by crossovers in the interval between knob and telomere. They then went on to show that two major structural rearrangements on the short arm of chromosome 9, both of which nearly abolished recombination, nearly abolished the preferential segregation of a knob on the same arm.

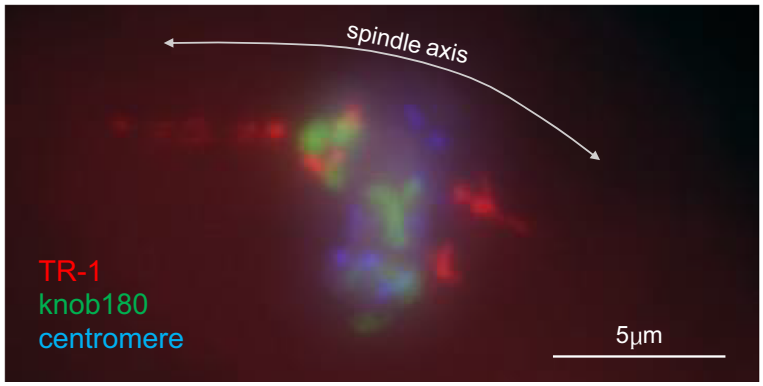
During the course of these studies, Rhoades and Dempsey discovered that Ab10 increases recombination throughout the genome. They first noticed that Ab10 caused a ~ 50% increase in recombination in the pericentromeric region of chromosome 3. Others obtained similar data for chromosome 9 (Kikudome 1959) and the pericentromeric regions of chromosomes 5 and 10 (Robertson 1968; Miles 1970). The effect was also observed when large paracentric inversions were paired with normal chromosomes; within such inversions, the pairing was visibly improved in the presence of Ab10 (Gillies 1973) and recombination was elevated by as much as 4–fivefold (Rhoades and Dempsey 1966). The factor(s) responsible for the recombination effect have been localized to a region that includes part of the large knob (Miles 1970; Hiatt and Dawe 2003a). We have speculated that the "recombination effect" is an important component of the drive system that helps to assure recombination in centromere-knob intervals (Ghaffari et al. 2013), but in the absence of mutants or variants that lack the recombination effect, this proposition is difficult to prove.

The Rhoades model for meiotic drive

Rhoades envisioned a model for the meiotic drive (Fig. 1A) that remains supported by all available evidence (Rhoades and Others 1952). First, recombination must occur between centromeres and knobs to yield chromosomes composed of one chromatid with a knob and the other without a knob (a heteromorphic


A
Prophase I
Anaphase I
Metaphase II
Anaphase II
Egg


B
TR1 knobs
180 bp knobs
N10
R
WOL Sr
Ab10-I
R
LOW Sr
Trkin
Kindr
K10L2
R
Trkin
Ab10-II
R
LOW Sr
Trkin


C
spindle axis
TR-1
knob180
centromere
5μm

◂ **Fig. 1** The Ab10 haplotype and its phenotypes. **A** The Rhoades model for meiotic drive. Recombination frequently occurs between centromeres and knobs to create heteromorphic dyads. Neocentromeres draw knobbed chromatids towards the poles at anaphase I. At metaphase II, spindles initiate around chromosomes, and neocentromeres form on the nascent spindles, pulling knobs towards the upper and lower poles and potentially swinging linked centromeres in the same direction (detailed images showing how swinging might occur are in Swentowsky et al. 2020). Ultimately, knobs on recombinant chromosomes lie in the upper or lower cells of the linear tetrad. Only the lower cell will go on to become the egg. TR-1 is shown in red, knob180 in green, and centromeres in yellow. Dashed lines represent spindle microtubules. **B** Structure of Ab10 and K10L2 as compared to N10. The Ab10 haplotype begins at the left edge of the first TR-1 rich knob (purple arrow, see also Liu et al. 2020); to the right of this point, all sequence is either novel or inverted relative to N10. The two inversions of sequence with homology to N10 are indicated by blue lines. We originally observed eight *Kindr* genes (Dawe et al. 2018) then found a ninth (Liu et al. 2020), but a more recent assembly demonstrates there are at least ten (the new assembly is not yet published). The K10L2 chromosome contains *Trkin* but we do not know its location relative to the two TR1-rich knobs. Ab10-II does not have a function copy of *Trkin* (Swentowsky et al. 2020). The names of the classical genes on Ab10 are shortened: R is *R1*, L is *L13*, O is *O7*, W is *W2*, and Sr is *Sr2*. **C** TRKIN-driven TR-1 neocentromeres. This metaphase II cell is from the Ab10-*smd1* mutant, where *Kindr* is non-functional and knob180-neocentromeres are absent. In mutants lacking *Kindr*, TR-1 neocentromeres are particularly dramatic, as shown here, where red streaks of TR-1 sequence are flowing out with the spindle towards the poles. The TR-1 repeats, knob180 repeats, and CentC, a centromere repeat, are labeled using fluorescent oligonucleotides. The chromosomes are also shown in a light gray color. This image was collected by Lisa Kanizay as a part of her dissertation research

dyad). Neocentromere activity in meiosis I then pulls the knobbed chromatids rapidly towards spindle poles, where presumably they will stay throughout the subsequent interphase (positions of knobs after anaphase I do seem to be stable, at least in male meiocytes; (Dawe and Cande 1996)). Spindle formation in plants occurs by a self-assembly process that initiates around chromosomes and flows out to form poles (Zhang and Dawe 2011). It is reasonable to presume that the poleward orientation of knobs set up in anaphase I will favor the orientation of knobs towards the upper and basal cells in meiosis II. Neocentromeres initiate movement early in spindle formation so that the pulling forces can (in principle) swing linked sister kinetochores towards the same poles, reducing the likelihood that centromeres and knobs will travel in opposite directions (Yu et al. 1997; Swentowsky et al. 2020). Since only the basal cell will become the egg, this mechanism assures that knobs on recombinant chromosomes will be transmitted to the next generation. Since the maximum frequency of heteromorphic dyads is ~ 66% (considering all possible exchanges among four chromatids (Hall and Dawe 2017)), the maximum meiotic drive is ~ 83% (half the non-recombinants segregate to the egg by chance). Most Ab10 types show less than 83% drive, but three isolates of Ab10 (Ab10-III-Caq, Ab10-III-Gua, and Ab10-II-Oax) come close to reaching this theoretical maximum (Higgins et al. 2018).

The main weakness of the model is that it has never been directly visualized in female meiosis where meiotic drive occurs. All published images of neocentromere activity are from male meiotic cells, which are much easier to collect and analyze. Inna Golubovskaya, who was gifted in preparing specimens in this difficult cell type (Golubovskaya et al. 1992), once showed me an image of neocentromere activity during female meiosis but that image has been lost. Ideally, the key elements of the model that (1) knobs from heteromorphic dyads are almost always preferentially segregated and that (2) neocentromeres from meiosis I retain their trajectories and continue to orient towards the outermost cells would be confirmed either by careful analysis of fixed cells or some form of live-cell visualization. It remains possible that drive is not entirely dependent on these two events, but that there is also some form of biochemical gradient that facilitates the movement of knobs to the basal megaspore (Swentowsky et al. 2020).

Structure of Ab10

Cytological structure

Most of what is known about the structure of Ab10 was learned by cytogenetics alone. For decades, Rhoades and his students had little else to work with besides a light microscope and clever genetic tricks that produced deletions and other visible alterations of Ab10. Rhoades established early on that the unique features of Ab10 are limited to the region distal to the *R1* gene (Rhoades 1942). All sequence about 1–2 cM

to the right of *R1* on Ab10 displays no recombination with normal chromosome 10 (N10) (Kikudome 1959) and is referred to as the Ab10 haplotype. The major features of Ab10 are, starting next to *R1*, three small knobs composed of TR-1 repeats, an extended euchromatic domain, a very large knob composed of knob180 repeats, and a distal euchromatic region (Fig. 1B).

A large number of genes distal to *R1* on N10 occur on Ab10 as well, although in reordered form. Within this region are several easily scorable morphological markers, including *White2* (*W2*), *Opaque7* (*O7*), *Luteus13* (*L13*), and *Striated2* (*Sr2*). Rhoades and Dempsey had discovered that in some genetic backgrounds carrying B chromosomes ("high-loss" lines), knobs fail to separate at anaphase and cause breakage of the arms carrying knobs (Rhoades and Dempsey 1972, 1973). They used a high-loss line to induce breakage at the large knob on Ab10 and loss of the distal of *Sr2* marker (Rhoades and Dempsey 1985). Several simple terminal deficiencies were recovered by this means, which they characterized in detail. The data showed that the order of the genes on Ab10 is altered relative to N10; instead of *W2-O7-L13-Sr2*, the order on Ab10 is *L13-O7-W2-Sr2*. Restriction mapping confirmed the *W2-O7-L13* inversion and also identified a second smaller inversion (Mroczek et al. 2006). The presence of two inversions and an extensive novel sequence explains why Ab10 does not recombine with N10.

The classic studies of Ab10 were carried out with a single accession obtained outside of Mexico City, which we call Ab10-I-MMR (for Marcus M. Rhoades). However, a second type of Ab10, called Ab10-II, has been known since the 1930s. Ab10-II is common in teosintes (the progenitor of maize) but is apparently rare in cultivated maize (Longley 1937; Kato 1976; McClintock et al. 1981) (Fig. 1B). Both Ab10-I and Ab10-II show preferential segregation, induce neocentromeres, increase recombination in pericentromeric areas, and contain the inversion of *W2-O7-L13* (Rhoades and Dempsey 1988a, b, 1989). Later surveys revealed a third cytological form (Ab10-III) that is similar to Ab10-I but distinguished by TR-1 repeats in the large knob (Kanizay et al. 2013b). More variations of Ab10 almost certainly exist. Ab10 is found in about 6–15% of all maize landraces and teosinte plants (McClintock et al. 1981; Kanizay et al. 2013b) yet we have only collected and analyzed nine (Higgins et al. 2018). Ab10 has not been observed in modern inbreds, presumably because of the deleterious fitness consequences when homozygous (see below).

Molecular structure

The Ab10-I-MMR haplotype has recently been sequenced and assembled (Liu et al. 2020). The three small knobs are fully assembled (4.2 Mb, 2.6 Mb, and 2.1 Mb in size) and are indeed composed entirely of TR-1 repeats. The two inversions containing sequences shared with N10 are 4.4 and 8.3 Mb in size. The large knob, which may be as large as ~ 30 Mb, is only partially assembled. The rest of the Ab10 haplotype (~ 22.4 Mb) is relatively gene sparse and does not appear to have syntenic homology to any other maize chromosome.

Mechanism of neocentromere activity

Rhoades for most of his career believed that the large knob on Ab10 itself activated neocentromeres, although by what means he never ventured (Rhoades and Others 1952; Rhoades and Dempsey 1985). This long-held belief explains why he and his students continued to refer to Ab10 as "K10," when, by common nomenclature, the "K" designation applies to the knob only (for instance the knob on chromosome 9S is K9S). He had a high regard for the mysterious properties of heterochromatin, partly due to his other work on how heterochromatin could break chromosomes, alter recombination, and induce nondisjunction in both cis and trans in some lines (Rhoades 1978). It was not until 1986 that Rhoades and Dempsey stated they were no longer convinced that there was anything special about the K10 knob, accepting that there must be something proximal to the knob that could activate neocentromeres (Rhoades and Dempsey 1986). By 2002, we had established that there are two neocentromere-activating factors, one located near the three small TR-1-rich knobs and another located close to the large knob180-rich knob (Hiatt et al. 2002). The corresponding genes are now known as *Kinesin driver* (*Kindr*), which powers knob180 repeats, and *TR-1 kinesin* (*Trkin*), which powers TR-1 repeats (Dawe et al. 2018; Swentowsky et al. 2020). Both are microtubule-based molecular

motors of the kinesin-14 class that move cargo towards microtubule minus ends, which in spindles, are located at the poles.

Kindr

We identified *Kindr* as the most abundantly expressed sequence from the distal tip of Ab10. *Kindr* is encoded by a family of ten tandemly-arrayed copies spread over a megabase of sequence in the distal tip (Dawe et al. 2018; Liu et al. 2020). To demonstrate the function of *Kindr*, we took advantage of prior mutant screens that generated a collection of five mutants that appeared to have complete Ab10 haplotypes but failed to show meiotic drive (Dawe and Cande 1996; Hiatt and Dawe 2003a; Dawe et al. 2018). Analysis of *Kindr* expression revealed that two of the mutants, Ab10-*smd1* and Ab10-*smd12*, showed vastly decreased expression of *Kindr*. In both mutants, the *Kindr* genes were methylated over promoters and gene bodies in a pattern that is consistent with gene inactivation at the epigenetic level. Mutants of this type are referred to as epimutants. We went on to create a *Kindr* RNAi knockdown, which ultimately led to the isolation of a third *Kindr* epimutant that showed no detectable meiotic drive (RNAi can induce stable changes in DNA methylation in plants through a process known as RNA-dependent methylation (Sigman et al. 2021).

The closest homologs of *Kindr* within the maize genome are *Divergent spindle1* (*Dv1*) (Higgins et al. 2016) and *Varied-kernel-size phenotype1* (*Vks1*) (Huang et al. 2019), both of which function in spindle formation by facilitating the bundling of microtubules. These canonical Kinesin-14 s have two microtubule-binding domains, where the motor is on the C-terminal end and a second microtubule-binding domain is on the N-terminus. KINDR differs from its closest homolog VKS1 primarily in the N-terminal cargo-binding end, suggestive of a novel binding function. Within the motor domain KINDR shows excellent homology to other kinesin-14 s and functions as an active kinesin in vitro (Dawe et al. 2018). Immunolocalization experiments demonstrated that KINDR localizes specifically to knob180 repeats, and not TR-1 repeats, during meiosis (Dawe et al. 2018).

These data established that *Kindr* is required for meiotic drive and strongly implicated KINDR as the molecular motor that moves knobs containing knob180 repeats to poles. The question of how KINDR recognizes knob180 repeats specifically has not been answered. Gel shift assays have failed to show any sequence-specific binding between KINDR and knob180 repeats (Swentowsky 2021), suggesting that KINDR binds to another protein that in turn binds to DNA. A likely candidate is a gene defined by the mutant Ab10-*smd13*, one of our five mutants of meiotic drive. Unlike the other mutants, Ab10-*smd13* shows a normal expression of *Kindr* and contains the complete *Kindr* complex. In the Ab10-*smd13* mutant, KINDR does not localize to knobs, suggesting the gene(s) may encode the predicted adapter protein (Swentowsky 2021). Experiments are underway to identify the Ab10-*smd13* gene product.

Trkin

Trkin was identified as a novel kinesin-14 located between the first and second TR-1 knob of the assembled Ab10 haplotype (Swentowsky et al. 2020). Unlike *Kindr*, *Trkin* is only present in one copy and is not ancestrally related to *Kindr*. While the coding sequence is of moderate size (~1700 bp), the gene is over 130 kb in length, with many large introns riddled with transposons. It is one of the longest genes in maize. The encoded protein is also remarkably divergent, sharing only 43% protein homology to its closest homolog DV1, but retains active motor activity in vitro. Immunolocalization demonstrated that TRKIN binds exclusively to TR-1 repeats and not to knob180 repeats, in accordance with expectations from genetic data. However, further interpretations about the role of *Trkin* are complicated by the fact that two known Ab10 variants (Ab10-II-MMR and Ab10-I-Pue) lack functional *Trkin* (and TR-1 neocentromeres) but still show high levels of the meiotic drive (Mroczek et al. 2006; Swentowsky et al. 2020) (Table 1). We explained this by arguing that the *Trkin*/TR-1 system can facilitate the action of the *Kindr*/knob180 system when they are present in the same knob (which is the norm (Swentowsky et al. 2020; Hufford et al. 2021)). TR-1 neocentromeres look very different from knob180 neocentromeres (Fig. 2C). Unlike knob180 neocentromeres, TR-1 neocentromeres appear earlier in the cell cycle and stretch out, sometimes covering the entire distance of a half spindle (Hiatt et al. 2002; Swentowsky et al. 2020). We argued that when TR-1 and knob180 are mixed together this early action can

Table 1 Observed meiotic drive with various Ab10 crosses

Female genotype	Kinesins/knobs[1]	Segregation[2]
Ab10-I-MMR	Trkin 🔴 Kindr 🟢	~71-79%
N10	- -	
Ab10-II-MMR	- 🔴 Kindr 🟢	~70-79%
N10	- -	
Ab10-I-*smd12*	Trkin 🔴 - 🟢	~49%
N10	- -	
K10L2	Trkin 🔴 -	~51-52%
N10	- -	
Ab10-I-MMR	Trkin 🔴 Kindr 🟢	~52-54%
K10L2	Trkin 🔴 -	
Ab10-II-MMR	- 🔴 Kindr 🟢	~56-60%
K10L2	Trkin 🔴 -	

[1]TR-1 knobs are indicated in red and knob180 knobs are indicated in green

[2]Segregation for the haplotypes over the bars. The males in all crosses were standard N10 tester lines. All data are from Kanizay et al. (2013a), except for the Ab10-I-*smd12* cross, which is fromDawe et al. (2018)

help to orient knobs towards the basal cell in meiosis II (Swentowsky et al. 2020).

While the contribution of *Trkin* to Ab10-mediated meiotic drive may be subtle, it remains possible that *Trkin* can act alone on TR-1 repeats to promote a significant level of drive. Evidence in favor of this hypothesis comes from the analysis of two closely linked knobs at the end of chromosome 10L that are together referred to as K10L2 (Fig. 2B). The knobs are composed entirely of TR-1 repeats and are linked to *Trkin* (Kanizay et al. 2013a; Swentowsky et al. 2020). Large-scale testcrosses where K10L2 was heterozygous with N10 demonstrated weak levels of the meiotic drive (~51–52%), which at the time we were not impressed with (Kanizay et al. 2013a, Table 1). However, I have since rediscovered older literature that further supports an independent role of *Trkin* in promoting drive. The first set of data are from Margaret Emmerling (who worked with both Rhoades and Lewis Stadler). Using X-rays, she fortuitously created a ring chromosome from Ab10 (Emmerling 1955), where one break occurred very close to the end of the short arm and the second in the middle of the large knob. She later identified linear derivatives of the ring (Emmerling 1959), one of which (K^0) contains the three small knobs but not the large knob, and the second (K^s) contains the three small knobs and about half of the large knob. Based on structure, these variants presumably contained *Trkin* but lacked *Kindr* (this cannot be confirmed since they are now lost). She then went on to test whether either chromosome could trans-activate meiotic drive at a large knob on chromosome 9S (TR-1 repeats are visible by FISH in most but not all 9S knobs (Albert et al. 2010)). The data show that K^s and K^0 caused 53.5% and 53.2% preferential segregation of a gene tightly linked to K9S. More extensive data can be found in the PhD dissertation of Judith Miles, a student of Rhoades (Miles 1970). She created six additional Ab10 deletion derivatives from Emmerling's ring chromosome, all of which contain the three small knobs and part of the large knob (presumably containing *Trkin* but not *Kindr*). She then tested each for their capacity to trans-activate drive at both the 9S knob and a knob on chromosome 3L (which has both knob180 and TR-1 repeats (Albert et al. 2010)). The results from many crosses assayed at two separate knobs are convincing, showing drive on average of ~55% at K9S and ~58% at K3L (these numbers are averages from Table 3-XIII in (Miles 1970)). Emmerling and Miles also checked whether the Ab10 deletion variants themselves show meiotic drive over N10, and observed very little (51–52%) or none. However, these data are misleading because Ab10 mutants that are defective for *Kindr* (such as Ab10-Df(L) and Ab10-*smd12*) show reduced segregation below Mendelian (~47% and 49%) (Hiatt and Dawe 2003b, a; Dawe et al. 2018; Table 1). We assume deleterious alleles in the Ab10 haplotype impair normal transmission through the gametophyte and this effect is normally masked by meiotic drive.

In summary, extensive genetic data suggest that *Trkin* alone can cause meiotic drive of knobs with TR-1 repeats. This implies that K10L2, with its linked *Trkin* gene, can be accurately viewed as a meiotic drive haplotype—albeit a far less effective meiotic drive haplotype than Ab10. The extreme protein level divergence of TRKIN relative to KINDR, VKS1, and DV1 further suggests that the *Trkin*/TR-1 system may be much older than the *Kindr*/knob180 system. One way to explain the existence of both neocentromere systems on Ab10 would be to postulate that the *Trkin*/TR-1 haplotype evolved first and was later modified by the addition of *Kindr* (and *Smd13*) and knob180 repeats to complete the *Kindr*/knob180 system.

Evolutionary impact

Although Ab10 is an excellent driver, it is only observed in about 6–15% of sampled individuals (Kato 1976; McClintock et al. 1981; Buckler et al. 1999; Kanizay et al. 2013b), consistent with it having significant deleterious fitness consequences (Buckler et al. 1999). Gametic selection against pollen containing Ab10 is one possible explanation. In support of this view, Rhoades demonstrated that when lines heterozygous for Ab10-I were crossed as a male, only 42% of the progeny contained Ab10 (Rhoades 1942). However, this was not true for Ab10-II which was transmitted at Mendelian levels through the male (Rhoades and Dempsey 1988b). In a more thorough study (Higgins et al. 2018), we observed minimal deleterious effects when Ab10 is heterozygous but significant reductions in male fertility, seed number, and seed size when Ab10 is homozygous. The reasons for this are not clear, but may suggest that Ab10 does not contain the complete complement of genes that are normally present on N10 (Higgins et al. 2018). Additional modeling showed that when the main fitness effects are recessive, the likelihood of Ab10 invading a population is very high, but its spread within the population will be limited by the negative consequences of homozygosity (Hall and Dawe 2017). The predicted and observed population frequencies of Ab10 are in rough agreement, though there may be deleterious effects on other fitness components that were not measured in our greenhouse and field studies (Hall and Dawe 2017; Higgins et al. 2018).

In populations where Ab10 is abundant, there is likely to be a corresponding increase in the overall frequency of knobs (Longley 1945). An analysis of extensive data on knob location and size (Kato 1976) demonstrated a strong positive correlation between Ab10 and overall knob abundance (Buckler et al. 1999). Meiotic drive also helps to explain why knobs are so large: larger knobs show higher levels of meiotic drive than smaller knobs, and when paired against each other, a large knob preferentially segregates over a small knob (Kikudome 1959). Knob repeats can make up as much as 20% of total genome size (> 500 Mb; (Dawe et al. 2018)) and explain most of the observed variation in genome size among maize inbreds (Chia et al. 2012). The meiotic drive also helps to explain the locations of knobs (Longley 1939; Buckler et al. 1999). Knob repeats and small arrays can be found throughout the genome (Hufford et al. 2021) but arrays expand to massive size at only one or few "knob-forming" sites on each chromosome arm. In principle, any position that assures maximum recombination between centromere and knob should be acceptable as a knob-forming site. In maize and closely related teosintes (*Zea mays* spp. *parviglumis* and ssp. *mexicana*), knobs tend to lie in mid-arm positions. We have speculated that when knobs are in mid-arm locations they are more effective drivers because they are more likely to swing the linked centromere towards the same pole (Yu et al. 1997; Swentowsky et al. 2020). In one case where a knob on chromosome 3 was shifted to a more distal location (by a large inversion), drive was significantly reduced (Rhoades and Dempsey 1966; Buckler et al. 1999). In contrast, the knobs in distantly related species such as Zea *luxurians* and Zea *diploperennis* are located at or near telomeres (Albert et al. 2010). Assuming Ab10 is responsible for the frequency, size, and position of knobs (Buckler et al. 1999), the difference in knob positions is most likely due to differences in Ab10 haplotypes. Ab10 has been observed in Zea *luxurians* and Zea *diploperennis* (Kato and Lopez 1990; González and Poggio 2011) but never isolated and studied in detail. All knobs and Ab10 are less abundant at high altitudes, presumably due to selection on genome size (Poggio et al. 1998; Kanizay et al. 2013b; Bilinski et al. 2018).

Likely suppressors of meiotic drive

Given that Ab10 reduces fitness when homozygous and promotes genome size expansion when heterozygous, suppressors of Ab10-mediated meiotic drive are likely to have evolved (Hurst and Werren 2001). We know of two loci that may qualify as suppressors. The first is K10L2, which contains two TR-1 knobs and *Trkin* but lacks knob180 repeats and *Kindr*. K10L2 functions as both a weak meiotic driver and a suppressor of Ab10-mediated drive (Kanizay et al. 2013a, Table 1). When Ab10 was paired with K10L2 and testcrossed, Ab10 was only recovered in 52–60% of progeny while in controls where Ab10 was paired with N10, the drive was ~ 70–79% (Kanizay et al. 2013a). Similarly, Emmerling and Miles demonstrated that when Ab10 is paired with variants containing only the TR-1 knobs and *Trkin* (and lacking *Kindr*), the meiotic drive for Ab10 was reduced to ~ 54–65% (Emmerling 1959; Miles 1970). Presumably, the neocentromere activity promoted by K10L2, while barely enough to cause its own drive, is sufficient to compete with Ab10 in its poleward movement towards the future egg cell.

The second potential suppressor is a locus we refer to as *pseudo-Kindr* that is present at the end of the long arm of N10 (Dawe et al. 2018). In the B73 inbred, *pseudo-Kindr* is composed of six degenerate and truncated copies of *Kindr* in a duplicated and inverted orientation (Dawe et al. 2018). Different forms of *pseudo-Kindr* are also present in 25 other inbreds (Hufford et al. 2021). The array produces a large number of small RNAs (1.2% of siRNAs in developing B73 ears) that could, in principle, reduce the expression of *Kindr* or stably inactivate the *Kindr* complex in *trans*. The level of meiotic drive conferred by Ab10 can be quite variable (Rhoades 1942; Kikudome 1959). Compared to heterozygous Ab10/N10 lines, homozygous Ab10 lines show more dramatic neocentromeres (Rhoades and Others 1952; Snope 1967a) and promote slightly higher levels of the drive at unlinked knobs (Rhoades and Dempsey 1966). Natural epimutants of *Kindr* (Ab10-*smd1* and Ab10-*smd12*) were identified at a fairly high frequency (2/13000 plants), although it is impossible to know if they were induced by *pseudo-Kindr* or other forms of epigenetic inactivation.

Origin of Ab10 and generality of mechanism

It is natural to wonder if other plants or animals have meiotic drive systems similar to the Ab10 haplotype. Unfortunately, we have made no progress in interpreting the origin of Ab10 since the question was first posed by Longley (Longley 1938). At one point, it was argued that Ab10 may be derived from the maize B chromosome (Ting 1957); however, this was refuted based on a lack of significant pairing in haploid plants containing both chromosomes (Snope 1967b). We have now carried out sequence comparisons between the Ab10 haplotype (Liu et al. 2020), 26 complete maize genome assemblies (Hufford et al. 2021), and the B chromosome (Blavet et al. 2021) and see no regions of significant synteny outside of the regions shared with N10. Comparisons of *Kindr* and *Trkin* to all available plant sequences reveal no obvious close homologs, although this may change as additional genomes are completed. It is possible that most of the ~ 22.4 Mb of a novel sequence in the Ab10 haplotype was built from small pieces translocated from other chromosomes and millions of years of transposable element insertion, similar to the maize B chromosome (Blavet et al. 2021).

The fact that the *Kindr* and *Trkin* systems appear to be unique to maize is not unexpected—each meiotic drive system described to date has proven to be a story unto itself (Courret et al. 2019; Clark and Akera 2021). However, we might expect common themes. Kinesins, which have the power to alter microtubule dynamics and move chromosomes on spindles, may prove to be a common theme for many female meiotic drive systems (Clark and Akera 2021). A well-documented example of centromere drive in mice involves the activity of MCAK, a kinesin that destabilizes microtubules at the kinetochore interface to allow larger centromeres to orient towards the egg cell (Akera et al. 2019). The *Drosophila* chromatin-binding kinesin *nod* has been implicated as a meiotic driver that promotes the transmission of some chromosomes over others (and increases nondisjunction as a consequence (Zwick et al. 1999)). Similarly, supernumerary B chromosomes have evolved various selfish accumulation mechanisms and often encode kinesins (Blavet et al. 2021; Clark and Akera 2021). In the future, we can expect more quantitative mapping and sequence-based discovery of candidate

genes for potential meiotic drivers. Thanks in part to the dedicated work of Longley, Rhoades, and their many colleagues and students, kinesins are likely to be top candidates.

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