Meiosis-Driven Genome Variation in Plants

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Abstract: Meiosis includes two successive divisions of the nucleus with one round of DNA replication and leads to the formation of gametes with half of the chromosomes of the mother cell during sexual reproduction. It provides a cytological basis for gametogenesis and inheritance in eukaryotes. Meiotic cell division is a complex and dynamic process that involves a number of molecular and cellular events, such as DNA and chromosome replication, chromosome pairing, synapsis and recombination, chromosome segregation, and cytokinesis. Meiosis maintains genome stability and integrity over sexual life cycles. On the other hand, meiosis generates genome variations in several ways. Variant meiotic recombination resulting from specific genome structures induces deletions, duplications, and other rearrangements within the genic and non-genic genomic regions and has been considered a major driving force for gene and genome evolution in nature. Meiotic abnormalities in chromosome segregation lead to chromosomally imbalanced gametes and aneuploidy. Meiotic restitution due to failure of the first or second meiotic division gives rise to unreduced gametes, which triggers polyploidization and genome expansion. This paper reviews research regarding meiosis-driven genome variation, including deletion and duplication of genomic regions, aneuploidy, and polyploidization, and discusses the effect of related meiotic events on genome variation and evolution in plants. Knowledge of various meiosis-driven genome variations provides insight into genome evolution and genetic variability in plants and facilitates plant genome research.

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INTRODUCTION

Meiosis is a specialized cell division involved in gametogenesis, which governs the transmission of genetic material throughout sexual life cycles. It is characterized by two successive divisions with one round of DNA replication and the formation of four haploid daughter cells (Figs. 1 and 2) (also see [1] for a recent review of meiosis). At prophase of the first meiotic division (prophase I), homologous chromosomes pair, synapse, and recombine with each other and chiasmata form between non-sister chromatids in the paired homologous chromosomes (bivalent). Chiasmata hold two homologous chromosomes in a bivalent together until anaphase of the first division (anaphase I). At anaphase I, two homologous chromosomes in each of the bivalents separate and migrate to opposite poles. Each of the daughter cells receives one of the chromosomes at the end of the first division. This division reduces the chromosome number to half in the daughter cells. The second division is similar to mitosis, involving separation of sister chromatids and formation of four haploid daughter cells (Figs. 1 and 2). Mature gametes (eggs and sperm) developed from the haploid daughter cells fuse with each other to form diploid or polyploid offspring through fertilization. Hence, meiosis provides the cytological basis to genomic stability and integrity over sexual life cycles. On the other hand, meiosis induces genetic variations. At prophase I, recombination and crossing-over

occur between non-sister chromatids in each of the bivalents. This meiotic event shuffles the genetic material from paternal and maternal chromosomes in each of the bivalents. In addition, independent assortment and segregation of different pairs of homologous chromosomes at anaphase I result in different combinations of homologs in the daughter cells. Both meiotic events induce genetic variations. Meiosis, therefore, maintains stability and integrity of the genome and induces genomic variations as well.

Meiotic cell division is a dynamic cellular process controlled by a complex genetic network. Genetic, cytological, and immunochemical characterization of the meiotic process in model species, such as *Saccharomyces cerevisiae*, *Drosophila melanogaster*, and *Arabidopsis thaliana*, has led to the identification of genes conditioning distinct meiotic events, including recombination and crossing-over [2-4, see 5-7 for reviews], spindle assembly [see 8 and 9 for reviews], kinetochore orientation and chromosome segregation [10-13, see 14,15 for reviews], and cytokinesis [16,17]. Meiosis is a conserved cytological process and serves as a physical foundation for Mendelian genetics. Genes conditioning distinct meiotic events have been identified and characterized in plants [see 5-7 for reviews]. In recent years, plant species have attracted the attention of geneticists and cell biologists for the study of meiotic process and meiosis-driven genome variation because of the availability of increasingly more genetic and genomic resources in plants.

Meiosis determines the fate of chromosomes, including transmission and recombination, throughout the sexual life cycles in eukaryotes. Faithful transmission of chromosomes is ensured by the fidelity of meiotic process. Variant meiotic

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Fig. (1). Diagram of meiotic cell division and genome variations associated with distinct meiotic stages.

processes or meiotic errors result in various genomic variations, including variation in the chromosomal structure and number and the ploidy level [18,20-25, see 19,26 for reviews] (Fig. 1). Polyploidization and retrotransposon amplification have been considered two major mechanisms of genome expansion [18,27]. Recent studies indicate that variant meiotic recombination events result in deletion of retrotransposons and other repetitive sequences in plant genomes, suggesting those recombination events could be a mechanism to counteract retroelement and polyploidization-driven genome expansion [28-32]. In this review, we will concentrate on meiosis-driven genome variation in plants and discuss the effect of meiosis on plant genome evolution.

MEIOTIC RECOMBINATION AND GENOME VARIATION

Homologous chromosomes recombine with each other at prophase I and are held together by chiasmata resulting from crossing-over between non-sister chromatids. Two homologs in a bivalent segregate from each other when the chiasmata are resolved at anaphase I. Our knowledge of the mechanisms underlying meiotic recombination, homologous chro-

mosome pairing, and synapsis is still limited although significant progress has been made in this research area since the 1980s [20, see 5,6 for reviews]. Over the past two decades, advances in plant genomics, especially in *Arabidopsis thaliana* and rice, have dramatically enhanced our understanding of the structure and organization of plant genomes. Genetic and physical mapping of plant genomes suggest that many genes and DNA markers cluster in specific chromosomal intervals. Meiotic recombination events distribute unevenly within a genome and a chromosome in plants [33, see 19 for a review]. Recombination hot spots (chromosomal regions with higher recombination rates than the genome average) and cold spots (chromosomal regions with lower recombination rates than the genome average) have been identified in plant genomes [see 1,19,34-36 for reviews]. Higher recombination frequency has been observed within the gene-rich regions than those harboring repetitive DNA sequences in many plant species [see 1,6,19,34 for reviews]. Meiotic recombination can occur within the coding sequence of a gene (intragenic recombination) or within the sequence between genes (intergenic recombination). In addition, sequence similarity among members of a gene family or other

Fig. (2). Meiotic cell division of pollen mother cells in the tetraploid wheat (*T. turgidum*) genotype LDN at **a)** metaphase I, **b)** telophase I, **c)** metaphase II, and **d)** telophase II, showing chromosome pairing, synapsis, segregation, and spindle behavior.

tandem repeats could lead to unequal alignment of homologous chromosomal regions, and then unequal crossing-over.

Recombination between non-homologous chromosomal regions or non-homologous chromosomes, such as illegitimate recombination, results in deletions, duplications, inversions, and translocations. These meiotic recombination events could disrupt the function of a gene, generate new alleles at a gene locus, and cause variations in the genome structure and size. Recombination, therefore, is considered mutagenic [37]. Here, we will elucidate the effect of these meiotic recombination events on the variation and evolution of genes and genomes in plants.

Intragenic Recombination

In Mendelian genetics, it is assumed that a gene (“unit factor”) is transmitted as an intact heritable unit over generations. This assumption ensures Mendelian segregation ratios for a single gene and independent genes in hybridization experiments. Also, each linked gene is considered an intact heritable unit for linkage analysis and genetic mapping. In fact, intragenic recombination often occurs and results in disruption of a functional gene or generation of new alleles at the gene locus. Hence, some modification of the traditional concept of gene transmission may be required [38,39, see 40 for a review]. This type of recombination event usually complicate transmission genetic analysis of the genes involved, including molecular mapping, linkage analysis, and map-based gene cloning [41]. Meanwhile, intragenic recombination drives gene evolution in plants.

Intragenic recombination was first described in *Drosophila melanogaster* in 1940 [38] and later in the fungus *Neurospora* in 1955 [39]. Following these initial discoveries,

intragenic recombination has been observed and characterized in many other eukaryotes, including fungi, animals, humans, and plants. Point mutations have been considered a major driving force for gene evolution and the formation of novel alleles at a gene locus. In recent years, this concept seems to be changing because of more evidence demonstrating that intragenic recombination may also play an important role in gene evolution [46, see 42-45 for reviews] and the maintenance of population genetic variability in eukaryotes [47-50]. Higher intragenic recombination rates (recombination hotspots) than the genome average have been observed at a number of gene loci in plants, such as the *wx* locus in rice (*Oryza sativa*) [51] and maize (*Zea mays*) [52], the maize *Al* locus [53], and the maize *bronze* locus [54,55]. However, this seems not to be the case in *Arabidopsis*. Intragenic recombination rate at the *csr1* locus in *Arabidopsis* was found to be almost the same as the genome average [56]. Variation of the recombination rate among plant species might be associated with the differences in their genome structure and organization. It was also reported that transposable elements affect intragenic recombination in various ways [57]. Intragenic recombination could take place reciprocally or *via* a nonreciprocal process called gene conversion [49]. It could lead to the formation of novel functional alleles, truncated alleles, or pseudogenes at a gene locus.

Disease resistance genes are the major class of genes that have been cloned and extensively characterized in plants. Many disease resistance genes co-evolve with respective pathogens as described in the gene-for-gene model [58]. Genetic and sequence analysis of disease resistance genes suggests that intragenic recombination could be a mechanism for the generation of novel alleles conferring new resistance specificities in plants. Results from the studies of the maize

rust resistance gene complex *Rp1* demonstrated that recombination within this gene complex, mostly within the coding regions, led to new rust resistance specificities [59,60]. Over 30 rust resistance genes, designated *K*, *L*, *M*, *N*, and *P*, have been identified in flax (*Linum usitatissimum*). Extensive analysis of the *L* and *M* loci suggests that the *L* locus contains a single gene with multiple alleles and the *M* locus may contain about 15 related genes [61,62]. Only one gene was found to confer resistance specificity at the *M* locus. Three susceptible mutants were identified to have a deletion in the coding region of this gene, which probably resulted from unequal recombination of the repeats within the coding region of this gene [63,64]. Sequence and genetic analysis of 13 natural and *in vitro* engineered recombinant alleles at the *L* locus demonstrated that intragenic recombination resulted in mutant alleles that confer novel resistance specificities [65,66]. Many more studies on disease resistance genes, including the *Arabidopsis* downy mildew resistance gene *RPP8* [67], the tomato (*Lycopersicon*) leaf mold resistance gene *Cf-5* [68], the wheat (*Triticum*) leaf rust resistance gene *Lr21*, and the citrus (*Citrus*) tristeza virus resistance gene *Ctv* [69], revealed occurrence of the recombination within the coding region of disease resistance genes in plants. It is becoming more evident that intragenic recombination is a major force driving the evolution of disease resistance genes as described in the gene-for-gene model [58].

Intragenic recombination takes place at other gene loci in addition to the disease resistance genes. High recombination rates have been observed at some of the non-disease resistance gene loci in plants [51-55]. Molecular characterization of the maize *R* gene complex identified recombinant alleles derived from the intragenic unequal exchange between the genes in this complex [70]. Interestingly, a recent study of the sorghum (*Sorghum vulgare*) dwarf mutant *dw3* indicated that this mutant allele was generated by a direct duplication of an 882 bp interval in exon 5 of this gene. Instability of this mutant resulted from loss of the duplication due to unequal crossing-over between the duplicated regions. The intragenic unequal crossing-over event reverted the mutant allele *dw3* to the wild type allele *Dw3*, making this mutant unstable [71]. Hence, intragenic recombination generates allelic diversity, like point mutations, at gene loci and plays an important role in gene evolution.

Unequal Crossing-Over

Unequal crossing-over was first documented at the *Bar* locus in *Drosophila melanogaster* in the 1920s [72]. Following the discovery of this variant meiotic recombination, it was proposed that unequal crossing-over might be another factor resulting in gene mutation besides the point mutational changes in the nucleotide sequences of genes [37]. Over the past two decades, significant attention has been placed on this variant recombination event because evidence indicates that unequal crossing-over could be one of the major players for genome evolution and maintenance of genetic variability in natural populations. Recent advances in plant structural and functional genomics have significantly enhanced our knowledge of unequal crossing-over and its effect on the evolution of plant genomes. Repetitive DNA sequences, such as retrotransposons and gene families, comprise a large portion of the genome in many plant species [see 27,45,73

for reviews]. Misalignment between repeats during chromosome pairing and synapsis leads to unequal crossing-over resulting in deletions and duplications of repeats and related DNA sequences. Unequal crossing-over could also take place between sister chromatids [74,75]. Substantial research results have indicated that this type of variant recombination occurs frequently in plant genomes and may play an important role in plant genome evolution.

Genes with sequence similarity are often clustered within a small chromosomal interval in a genome. They are referred to as gene families because they are assumed to have arisen from a common ancestor. Numerous genes in plants, such as disease resistance genes, exist as members of gene families [70,76,77, see 44,45 for reviews]. More than 40 disease resistance genes have been cloned in plants [see 45,78 for reviews]. Many of them reside in gene families. Unequal crossing-over has been documented in a number of plant disease resistance gene families. Substantial evidence indicates that unequal crossing-over occurring within a disease resistance gene family results in novel haplotypes and novel resistance specificities. The maize rust resistance gene locus *Rp1* was identified to contain several *Rp1* homologs, some of which showed meiotic instability [79]. Sequence and genetic analysis identified deletions in the members of this gene family and chimeric genes (haplotypes) with various resistance specificities, demonstrating occurrence of unequal crossing-over between the homologs within this gene family [80,81]. The tomato leaf mold resistance gene *Cf-4* and *Cf-9* reside within a large gene family on the short arm of chromosome 1. Strong evidence indicated that unequal crossing-over-induced deletions of tandemly repeated genes resulted in novel haplotypes with different resistance specificities [82]. Unequal crossing-over points were found to locate primarily within intergenic regions [83,84]. Unequal crossover-driven gene evolution has been reported in a number of other disease resistance gene families across different plant species, including the gene families at the *Arabidopsis* locus *RPP5* [85], the soybean (*Glycine max*) loci *Rps* [86,87] and *Rsv1* [88], the lettuce (*Lactuca sativa*) *Dm3* locus [89,90], the barley (*Hordeum vulgare*) *Hv-elf4E* locus [91], and the citrus *Ctv* locus [69]. Similarly, unequal crossing-over takes place in gene families other than disease resistance gene families and generates novel haplotypes and alleles at those loci [70,74,75,92].

Unequal crossing-over can be intragenic or intergenic. Intragenic unequal crossing-over results mainly from duplications or repeats within coding regions, such as leucine-rich repeats (LRRs) in disease resistance genes [70,71,85]. Intergenic unequal crossing-over mostly occurs within gene families. Both types of unequal crossing-over cause deletions and duplications, generating novel alleles and haplotypes at the gene loci involved. It seems evident that unequal recombination widely occurs within a single gene or gene families even though the mechanism underlying this variant recombination event is still obscure. A better understanding of intragenic and intergenic unequal crossing-over may provide valuable insights into the mechanisms involved in the gene evolution.

Repetitive DNA sequences, including transposable elements and variable number of tandem repeats (VNTRs), comprise a large portion of the genome in plant species.

Over 50% of nuclear DNA is made up of repetitive sequences in large and complex plant genomes [93]. Retrotransposons are the major class of the repetitive DNA sequences in many plant genomes and are considered an important factor for genome evolution, especially for genome expansion [see 27 for a review]. Unequal recombination has been considered one of the mechanisms for genome contraction, which counteracts retrotransposon-driven genome expansion [28-30,32, see 18,27 for reviews].

Unequal crossing-over could occur within LTR (long terminal repeat)-containing retrotransposons due to the LTRs at both ends of the element. This variant recombination event removes the internal domain of the retroelement and leads to solo LTRs [94]. Sequence analysis of a contiguous 66-kb barley DNA fragment identified several types of retroelements, most of which were solo LTRs. Results from this study suggested that unequal recombination and intraelement recombination between LTRs led to the deletion of the internal components in the integrated retroelement and the formation of the solo LTRs [28]. Investigation of 1,000 elements from 11 LTR retrotransposon families in the rice genome revealed that more than three-quarters of the elements were either solo LTRs or truncated fragments. It was predicted that over 190 Mb of LTR retrotransposon sequences have been removed from the rice genome in the last eight million years [32]. Another study with three LTR retrotransposon families in the rice genome identified solo LTRs in a different percentage. It appears that the ratio of solo LTRs to intact LTR retroelements varies with the retrotransposon families in the rice genome [29]. Both LTR retrotransposon studies demonstrated that the solo LTRs and truncated elements in the rice genome originated primarily from unequal recombination [32,29]. Sequence deletion in the LTR retrotransposons due to unequal recombination was also considered one of the mechanisms involved in wheat genome evolution [30]. Most retroelements investigated in the maize genome, however, were found to be intact [95]. There might be another mechanism that counterbalances genome expansion by retrotransposon amplification in maize.

Microsatellites, also called simple sequence repeats (SSRs), are another class of widespread repetitive sequences in the genomes of both prokaryotes and eukaryotes. This type of short repeat is often associated with non-repetitive DNA in plant genomes. They reside primarily within or near genes [96]. Unequal crossing-over may be one of the major mechanisms responsible for the variation and instability of microsatellite loci [97-100]. Since microsatellite loci are usually located near or within genes, unequal crossing-over between the short repeats in the microsatellites may lead to novel alleles at microsatellite loci and the gene loci involved. Unequal crossing-over, therefore, could be the driving force behind the evolution of microsatellites and their associated genes.

Illegitimate Recombination

Illegitimate recombination is the recombination occurring between non-homologous DNA sequences with only a few identical nucleotides. Retrotransposon amplification and polyploidization have been thought to be two major mechanisms underlying genome expansion in plants [18,94]. A few

lines of evidence suggest that illegitimate recombination is probably another major force to shrink genomes, counteracting genome expansion in addition to unequal crossing-over in plants [30-32]. Illegitimate recombination is characterized by the involvement of short repeats in the recombination events. Frequent deletion of short repeats in *Arabidopsis*, rice, and wheat retroelements suggested the engagement of illegitimate recombination in genome contraction, which might counteract genome expansion due to retrotransposon amplification [30-32]. Apparently, more direct evidence is needed to confirm the effect of illegitimate recombination on plant genome evolution.

Substantial evidence demonstrates that meiotic recombination is a major process to shuffle DNA sequences and to reshape the genome. Recombination frequency is not even throughout a genome [see 1,19,34-36 for reviews]. Hence, location and structure of genes or non-genic sequences determine their fate in evolution. DNA sequences, including genic and non-genic sequences, residing in a recombination "hot spot" may be less conserved than those in a recombination "cold spot". For example, meiotic recombination is restricted within and near centromeres and telomeres, which may explain why centromeric and telomeric sequences are more conserved than DNA sequences in other genomic regions [101].

MEIOTIC CHROMOSOME SEGREGATION AND ANEUPLOIDY

Homologous chromosomes pair, synapse, recombine, and segregate at the first meiotic division and sister chromatids segregate at the second meiotic division (Figs. 1 and 2). A number of genes have been identified to condition the distinct meiotic events in yeast, animals, humans, and plants [2,102, see 1,5-9 for reviews]. Abnormalities of chromosome segregation-related meiotic events due to gene mutation or other factors may lead to the formation of chromosomally imbalanced gametes and aneuploids in the offspring (Fig. 1) [20-23]. Here, we will focus on asynapsis- and desynapsis-induced aneuploidy in plants.

Proper chromosome pairing, synapsis, and recombination are prerequisites for accurate segregation of homologous chromosomes at meiosis I. Synapsed homologous chromosomes (bivalent) are held together until anaphase I by the chiasmata resulting from crossing-over between non-sister chromatids in the bivalent and the cohesion protein (cohesin) [10,13,103-106]. Monopolar attachment of microtubules to the sister kinetochores at metaphase I is another prerequisite to ensure accurate segregation of homologous chromosomes at meiosis I [14,107]. At anaphase I, chiasmata are resolved and cohesion proteins on the chromosome arms are removed. Microtubules attached to each of the two sister kinetochores in the bivalent pull the two homologous chromosomes into opposite poles and each of the two daughter cells receives one member from each of the homologous chromosome pairs at the end of meiosis I. Centromeric cohesion, however, is preserved to hold two sister chromatids together until anaphase II [10,103]. Bipolar attachment of the microtubules from opposite poles to the sister kinetochores ensures equational division of sister chromatids at meiosis II. Hence, pairing, synapsis, and recombination between homologous

chromosomes and orientation of sister kinetochores at both meiotic divisions govern chromosome segregation and transmission throughout meiosis (Fig. 2).

Homologous chromosomes may fail to pair or synapse with each other due to genetic or environmental factors. This phenomenon is termed asynapsis. Alternatively, homologous chromosomes pair or synapse with each other normally, but the association cannot be held until anaphase I and they separate prematurely. This variant meiotic process is termed desynapsis (Fig. 1). Asynaptic and desynaptic mutants have been documented in many plant species [see 108 for a review]. Some of the mutants have been extensively characterized in major crop and model species, including wheat [109], maize [see 110 for a review, 111], rice [112-115], tomato (*L. esculentum*) [116], soybean [117], and *Arabidopsis thaliana* [118-122]. Asynapsis and desynapsis are usually conditioned by single recessive genes, such as *st2*, *st3*, and *st8* for asynapsis and *st4* and *st5* for desynapsis in soybean [117,123,124], *dy* and *dsy1* for desynapsis and *phs1* for poor homologous synapsis in maize [111,125], and *spo11-1-3*, *dsy1*, *mpa1*, and *asy1* in *Arabidopsis thaliana* [118-122]. In addition to single genes, duplicated recessive factors (*st6* and *st7*) for desynapsis were identified in soybean [126].

Both asynapsis and desynapsis lead to univalents (unpaired chromosomes) which are usually observed at metaphase I. Univalents either get lost or are randomly transmitted to daughter cells, resulting in chromosomally unbalanced gametes and eventually aneuploids in the offspring. In addition, univalents may undergo misdivision, such as transverse division, to produce telocentric, acrocentric, and acentric chromosomes or isochromosomes [127,128]. Abnormal spindles and cytokinesis have been found to associate with asynapsis and desynapsis in addition to abnormal chromosome behavior [129]. All these abnormal meiotic events associated with asynapsis and desynapsis induce variations in chromosomal structure and number.

Asynaptic and desynaptic mutants have been utilized to develop aneuploid stocks useful for genetic analysis. In common wheat (*T. aestivum*, $2n = 42$), a gene inhibiting asynapsis is located on the short arm of chromosome 3B [109], and thus the nullisomic for chromosome 3B is partially asynaptic. Seventeen monosomics and 11 trisomics were isolated from the progeny of nullisomic 3B in common wheat cultivar Chinese Spring [109]. It was reported that progeny of desynaptic plants in Jute (*Corchorus olitorius*, $2n = 14$) consisted of 9.24% primary trisomics, from which all of seven possible primary trisomics except trisomic 6 were isolated [130]. In soybean ($2n = 40$), a number of aneuploid lines with 41-43 chromosomes were isolated from different asynaptic and desynaptic mutants [131-133]. A set of soybean primary trisomics ($2n = 41$) were developed from these aneuploid lines [133]. They have been recently used to assign individual genes and molecular linkage groups to specific chromosomes [133-135].

MEIOTIC RESTITUTION AND POLYPLOIDIZATION

Normal meiosis includes two successive divisions of the nucleus preceding the formation of gametes. The first division is reductional and the second is equational. Failure of

the first or second division leads to the formation of restitution nuclei with unreduced chromosomes. If the first meiotic division fails at anaphase I, all the chromosomes stay on the equatorial plate to form one restitution nucleus with the same chromosome number as the mother cell at the end of meiosis I. The restitution nucleus usually undergoes normal second meiotic division. This variant meiotic process is called first division restitution (FDR). It is characterized by an equational division of the entire chromosome complement (as in mitosis) and the formation of two nuclei with unreduced chromosome number. A second variant meiotic process, called second division restitution (SDR), occurs when the first meiotic division proceeds normally, but the second division fails at anaphase II, resulting in two nuclei with unreduced chromosomes. Both FDR and SDR may occur simultaneously during the microsporogenesis and megasporogenesis, resulting in the formation of unreduced male and female gametes [see 26 for a review, 136]. The processes of normal meiosis, FDR, and SDR are diagrammed in Fig. (3).

Fig. (3). Diagram of FDR, SDR, and normal meiosis in a mother cell with one pair of homologous chromosomes.

Meiotic restitution, including FDR and SDR, has been documented in many plant species [25, see 26, 137 and 138 for reviews]. In angiosperms, more than 30% of species were estimated to be of polyploid origin [139,140]. Recent molecular studies have even revealed a polyploid origin of some classically considered diploid species, such as maize and soybean [141,142]. It has been suggested that functioning of the unreduced gametes produced through meiotic restitution may have been a major mechanism for the widespread occurrence of polyploidy in nature [24,137,139,143-150, see 26 for a review]. Meiotic restitution may also be a significant driving force behind speciation in plants.

Polyploidization is considered one of the major processes involved in plant genome expansion [18,94]. There are two major types of polyploids in plants, i.e. allopolyploids and

autopolyploids. Allopolyploids contain two or more chromosome complements which are different (non-homologous) from each other, whereas chromosome complements in the autopolyploid all are homologous. It appears that allopolyploidy is more prevalent than autopolyploidy in plants [151].

It is evident that allopolyploidy in plants originates through the spontaneous hybridization between genetically related species and subsequent chromosome doubling of the resultant hybrids *via* meiotic restitution and/or other mechanisms. An excellent example for elucidating allopolyploidization is the wheat species with different ploidy levels in the genus *Triticum* L. Common wheat, which is an allohexaploid with A, B, and D genomes, co-exists with at least two of its three diploid ancestors (*T. uratu*, $2n = 14$, AA genome; *Aegilops tauschii*, $2n=14$, DD genome) and its tetraploid ancestor (*T. turgidum*, $2n = 28$, AABB genomes). Strong evidence indicates that common wheat originated from the spontaneous hybridization between *T. turgidum* and *Ae. tauschii* about 8,000 years ago [152,153]. Meiotic restitution-induced unreduced gametes were observed in hybrids derived from the crosses between *T. turgidum* and *Ae. tauschii* and hexaploid wheat lines with doubled chromosomes ($2n = 42$, genomes AABBDD) were obtained from those crosses (Fig. 4) [136,146,149,154,155]. These research results demonstrate that meiotic restitution may play a vital role in allopolyploidization in plants. Allopolyploidization combines genomes from different species and significantly increases the genome size and complexity of the resulting species. Furthermore, recent studies indicate various genome modifications take place during polyploidization and subsequent diploidization, such as gene loss, changes in gene expression and epistatic interactions [151].

Autopolyploidy results from duplication of a single chromosome complement (genome). Involvement of meiotic restitution-induced unreduced gametes in fertilization has been thought to be a major mechanism for plant autopolyploidization in nature. Unreduced gametes due to meiotic restitution and/or other variant meiotic events and resultant autopolyploidy have been documented in many plant species [see 156 for review]. Spontaneous origin of autotriploids were reported in maize [157], tomato [158,159], sorghum [160], barley [161], rice [162], pearl millet (*Pennisetum americanum*) [163,164], durum wheat (*T. durum*) [165], and soybean [166,167], among others [see 156 for review]. It was likely that these autotriploids were derived from the fertilization of unreduced gametes (male or female) with normal reduced gametes (female or male). Autotetraploids of spontaneous origins have occasionally been observed among the offspring of meiotic mutants in several plant species, including soybean [168], *Oenothera gigas* [169], durum wheat [165], and maize [170]. Autopolyploids with ploidy levels higher than $4x$ are seldom observed in nature. As with allopolyploidization, autopolyploidization dramatically expands the genome size of a species by the duplication of an entire genome. Meanwhile, autopolyploidization causes genetic instability and complexity, especially with the autopolyploids having an odd number of chromosome complements.

Mechanisms underlying meiotic restitution are still very much obscure although more attention has been placed on

this complex meiotic process in recent years. Previous studies observed various abnormal meiotic events associated with meiotic restitution in plants and identified genes likely conditioning the events. For example, the wheat *msg* gene [165], barley *tri* gene [171], and maize *el* gene [172] were found to condition the formation of unreduced eggs, but not to affect the formation of normal haploid male gametes (sperm). In diploid alfalfa (*Medicago sativa*), two single recessive genes, *rp* (restitution pollen) and *jp* (jumbo pollen), condition $2n$ pollen formation by disorientation of spindles at metaphase II and failure of cytokinesis at the second division [173,174]. In the cultivated potato (*Solanum tuberosum*) and related diploid *Solanum* species, meiotic restitution appears

Fig. (4). Meiotic cell division of pollen mother cells in the F_1 hybrids of the two tetraploid wheat (*T. turgidum*) genotypes BEN and ISA with the *Ae. tauschii* accession RL5286, indicating FDR and the formation of unreduced gametes in the (BEN $\times$ RL5286) F_1 hybrid and regular meiosis in the (ISA $\times$ RL5286) F_1 hybrid.

to be associated with asynapsis and desynapsis [129,175], abnormal spindle orientation at the second division [175-177], and abnormal cytokinesis [177]. A number of monogenic meiotic mutants that produce 2n pollen or 2n eggs in potato have been reported, including parallel spindles (*ps*), premature cytokinesis-1 (*pc-1*) and premature cytokinesis-2 (*pc-2*) [178], desynaptic (*ds-1*) and synaptic mutants (*sy-1*, *sy-2*, *sy-3*, and *sy-4*) [179], and omission of the second division (*os*) [180]. Different genetic systems for meiotic restitution were also observed in soybean [166,168,181-184]. Our results from recent studies in wheat suggest that failure of the proper attachment of microtubules with sister kinetochores in the first and second meiotic division may be the major factor resulting in meiotic restitution (Cai and Xu, unpublished).

Meiotic restitution generates allelic variations in addition to resulting in polyploidization. First division restitution is similar to mitosis and usually leads to unreduced gametes with the same genotype as the parent. Unreduced gametes derived from SDR, however, may be heterozygous at some loci because of meiotic recombination between non-sister chromatids at meiosis I if the parent is not a genetically pure line. Therefore, meiotic restitution may play an important role in both genome expansion and allelic diversity in plants.

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ABBREVIATIONS

VNTR	=	Variable number of tandem repeat
LRR	=	Leucine-rich repeat
LTR	=	Long terminal repeat
SSR	=	Simple sequence repeat
FDR	=	First division restitution
SDR	=	Second division restitution

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