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Epigenetic perspectives on the evolution and domestication of polyploid plant and crops

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Abstract

Polyploidy or whole genome duplication (WGD) is a prominent feature for genome evolution of some animals and all flowering plants, including many important crops such as wheat, cotton, and canola. In autopolyploids, genome duplication often perturbs dosage regulation on biological networks. In allopolyploids, interspecific hybridization could induce genetic and epigenetic changes, the effects of which could be amplified by genome doubling (ploidy changes). Albeit the importance of genetic changes, some epigenetic changes can be stabilized and transmitted as epialleles into the progeny, which are subject to natural selection, adaptation, and domestication. Here we review recent advances for general and specific roles of epigenetic changes in the evolution of flowering plants and domestication of agricultural crops.

Introduction

Polyploidy results from whole genome duplication (WGD), generating an organism or cell that has more than two sets of chromosomes. While polyploidy is rare in animals compared to plants, polyploid incidences occur frequently in amphibians, reptiles, fishes, and insects [1], in addition to the presence of two rounds of genome duplication in vertebrates relative to invertebrates [2]. The view about the evolutionary fate of polyploidy has been changed from the ‘dead-end’ [3] or occasional incidences [4] to contemporary innovation [5–7]. This is partly because the number of plant and animal species being sequenced has been increased dramatically. Estimates indicate that before the divergence of extant seed plants and angiosperms, two rounds of ancestral WGDs occurred, allowing selection and evolution of genes and pathways important to seed and flower development and eventually the dominance of angiosperms on the earth [6,8]. Counting against WGD, polyploids often undergo a diploidization process, including genome fractionation, reshuffling, gene loss,

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pseudogenization, and neofunctionalization [9,10]. Many of these polyploids are called paleopolyploids, and their chromosomes pair normally as diploids.

In addition to paleopolyploids, autopolyploids and allopolyploids are commonly formed (Figure 1). Autopolyploids result from WGD within a population of the same species, while allopolyploids are formed by hybridization between species followed by chromosome doubling or through fusion of unreduced gametes from different species [11,12]. Allopolyploid plants are generally more common than autopolyploids, which are related to disrupted chromosome segregation during meiosis, leading to a reduced fertility in autopolyploids. The low fertility problem also exists in newly formed allopolyploids, but it can be overcome over time, producing progeny and populations with competitive growth and reproductive advantages [11,13–15], in a condition known as amphidiploid or disomic diploid [12]. Compared with diploid plants, polyploid plants usually increase their cell size, consequently developing large organs, such as roots, leaves, flowers, and seeds [16]. This suggests an advantage for polyploids to develop complex agronomic traits that are selected and domesticated in polyploid crops [13], which may explain the common occurrence of polyploidy in crops, including wheat (*Triticum aestivum* L.) [17], cotton (*Gossypium hirsutum* L.) [18], oilseed rape or canola (*Brassica napus* L.) [19], banana (*Musa acuminata* L.) [20], and potato (*Solanum tuberosum* L.) [21], whose genomes are sequenced.

The genomic consequences and underlying mechanisms for generating evolutionary novelty and morphological diversity have been the focus of many recent studies (see reviews in [5,7,11,15,22–25]). Some changes are largely dependent on genetic and sequence variation, as observed in polyploids of *Brassica* [26,27•], *Tragopogon* [28,29], and wheat [30,31], while many others have an epigenetic basis, as seen in polyploids of *Arabidopsis* [32–34], cotton [35,36•,37•], and wheat [38,39].

In addition to the genetic changes, polyploidy is known to induce a multitude of epigenetic modifications [31], which include DNA methylation, histone modifications, and chromatin remodeling [12,22,40,41]. A partial list of chromatin modifications relevant to gene expression changes in polyploids and hybrids is shown in Table 1. DNA methylation is heritable epigenetic modifications for gene expression variation in plants and animals [42,43]. In plants, DNA methylation can occur in CG, CHG (H = A, T or C), and CHH sites [43]. DNA methylation in the coding regions is associated with the genes that are expressed at medium to high levels and enriched for housekeeping functions [44–46], while the methylation in the promoter regions is generally associated with gene repression or silencing. Moreover, CG methylation maintains centromere and chromatin stability [47], while CHG and CHH methylation that occurs in transposons and transposable element (TE) fragments associated with genes, resulting in silencing of genes and TEs or heterochromatin formation [48]. An exception is the positive association of small interfering RNA (siRNA)-directed DNA methylation (RdDM) [49] in the promoter regions with activation of the genes that are involved in developmental regulation, as observed in maize [50], cotton [51], and soybean [52]. Like DNA methylation, histone modifications mediate epigenetic regulation of gene expression, growth and development in plants and animals [40,42,53]. Some histone modifications, such as acetylation of histones H3 and H4 and trimethylation of H3 lysine 4 (H3K4me3), are known as euchromatic marks and often associated with active transcription,

whereas other modifications, such as methylation of H3K9 and H3K27, are known as heterochromatic marks and related to gene repression [53,54].

Like genetic variation, some epigenetic changes could form epialleles, which are defined as genes associated with stable DNA methylation or histone methylation marks that control heritable phenotypic traits [36•,55•]. Indeed, epialleles are associated with asymmetrical flower development in *Linaria vulgaris* [56•] and some QTLs in tomato such as fruit ripening [57•] and vitamin E accumulation [58]. Moreover, epigenetic variation within a population increases plant production compared with epigenetically uniform populations [59]. Hybridization and polyploidy can induce epigenetic changes that contribute to morphological and domestication traits during evolution [60]. The roles of epigenetic variation in the evolution and domestication of polyploid plants and crops are highlighted in this review.

Nonadditive gene expression and epigenetic regulation in interspecific hybrids and allopolyploids

A main question for molecular changes in interspecific hybrids and allopolyploids: is the expression of genes originating from different parents or progenitors additive or nonadditive? Nonadditive expression suggests that the expression level of a gene in a hybrid or allotetraploid is not equal to the average of the two parents or mid-parent value (MPV), namely, 1 plus 1 is not equal to 2, which can be larger than 2 (gene activation or upregulation) or less than 2 (gene repression, silencing or down-regulation) (Figure 1). Genome-wide nonadditive gene expression was first reported in the study of resynthesized *Arabidopsis* allotetraploids using DNA microarrays [61•], which revealed genome-wide expression dominance of *A. arenosa* over *A. thaliana* in resynthesized allotetraploids. Since then, the expression bias of homoeologs in different organs or tissues, including genome-wide expression dominance, has been documented in many other allopolyploid plants, including cotton [62], *Senecio* [63], *Tragopogon* [64], and wheat [65]. These nonadditive expression changes can lead to nonadditive or transgressive phenotypes and traits such as growth vigor and stress responses [66,67•,68].

Notably, the expression bias of subgenomes is also present in ancient polyploids as observed in *Arabidopsis* [69], maize [70•], and *Brassica rapa* [71], which is associated with biased TE distributions. A recent study reported that the expression dominance is established in the first generation hybrid of two *Mimulus* species [72], and the dominantly expressed subgenome is linked with lower levels of TE abundance and CHH methylation near the genes. However, the subgenomic expression dominance in interspecific hybrids or allopolyploids can depend on the tissues or organs examined during growth and development [18]. For example, expression bias of homoeologs is commonly observed in allotetraploid cotton [62]. In a recent survey of genome-wide gene expression among 35 different tissues and conditions, no overall expression dominance is found between A and D subgenomes, whereas in a given tissue or developmental stage, expression bias can occur up to 20–40% of homoeologous pairs [18].

Molecular mechanisms for nonadditive gene expression stem from the study of nucleolar dominance, which refers to biased expression of uniparental rRNA genes in an interspecific hybrid and allotetraploid [73]. Nucleolar dominance is an old epigenetic phenomenon that is widespread in plants and animals [74]. Chen and Pikaard found that transcriptional silencing of uniparental rRNA genes is associated with DNA methylation and histone deacetylation in the interspecific hybrids or allotetraploids of *Arabidopsis* [75] and *Brassica* [76••]. However, in the transient expression assay using protoplasts, both sets of parental rRNA genes are transcriptional active in allotetraploid *Arabidopsis* [75] and *Brassica* [77], but only one set of endogenous rRNA genes is expressed in *Arabidopsis* allotetraploids [75]. These results argue against the prevailing transcriptional dominance or enhancer competition model based on the study of *Xenopus* allotetraploids [78]. Further studies indicate roles for RdDM [79] in the establishment of nucleolar dominance. Similarly, asymmetrical silencing of rRNA genes in hexaploid wheat is accompanied by DNA methylation at CHG and CHH sites and histone methylation at H3K27me3 and H3K9me2 sites [80].

Epigenetic silencing of homoeologous protein-coding genes was first demonstrated in *Arabidopsis* allotetraploids, in which silenced protein-coding genes, such as *TCP3*, were derepressed by the treatment with 5-aza-2'-deoxycytidine (aza-dC) [32], a chemical inhibitor for DNA methylation. In subsequent studies, DNA methylation changes are more frequent in resynthesized *Arabidopsis* allotetraploids than the parents [81]; the aza-dC treatment in the allotetraploids has reactivated many genes, resulting in abnormal morphologies and development. Moreover, among different generations in the self-pollinating progeny gene silencing or activation is stochastic, and silenced genes are reactivated in the RNA interference (RNAi) lines for *met1* and *ddm1* in *Arabidopsis* allotetraploids [33]. Notably, in the *Arabidopsis* allotetraploids between *A. thaliana* and *A. arenosa*, demethylation by RNAi-*met1* has larger effect on activating transposons, centromeric RNAs, and protein-coding genes of *A. thaliana* origins than those of *A. arenosa* origins [82]. This suggests differential epigenetic modifications between two subgenomes within the allotetraploid, which is consistent with genome-wide dominance of *A. arenosa* genes over *A. thaliana* ones [61••]. A recent study in the interspecific hybrid between *A. thaliana* and *A. lyrata* also found overall down-regulation of *A. thaliana* genes compared to *A. lyrata* genes, which correlates with *A. thaliana* chromatin that is more compact than *A. lyrata* chromatin [83], and the *A. thaliana* genes that are associated with histone H3K27me3 marks tend to alter their expression in the interspecific hybrid.

Besides the groundbreaking work in *Arabidopsis*, genome-wide DNA methylation changes are also observed in newly synthesized allotetraploid *B. napus* [27•] and domesticated canola [19]. In hexaploid wheat, although DNA methylation levels are similar across three progenitor's genomes, differential methylation exists between the subgenomes with similar proportions, which shows a negative correlation between subgenome-specific promoter methylation and decreased levels of gene expression [84]. In addition to epigenetic changes in polyploids, aneuploidy can also induce changes in gene expression and epigenetic regulation [85]. In hexaploid wheat aneuploids, although low levels of nucleotide sequence changes are observed, cytosine DNA methylation patterns change dramatically in all homeologous group 1 whole-chromosome aneuploidy lines examined, with monosomic 1A (missing chromosome 1A) showing the largest amount of methylation changes [85].

Epigenetic variations contribute to plant evolution and crop domestication

Epigenetic changes can lead to phenotypic variations during plant evolution. In *L. vulgaris* normal plants exhibit bilaterally symmetrical flowers, while radially symmetrical flowers are associated with a naturally occurring epimutation [56•]. The epiallele is related to DNA hyper-methylation of the promoter regions in the *Linaria cycloidea* (*Lcyc*) locus that is responsible for bilateral symmetry of flower development. This epimutation led Carolus Linnaeus 270 years ago to classify the *Peloric Linaria* inflorescence in a species different from regular *L. vulgaris*. This type of epimutation could be widespread in natural and experimental populations [86] and exist as stable alleles including *FWA* that controls flowering time in *Arabidopsis* [87••] or quantitative trait loci (QTLs) associated with agronomic traits [55••]. For example, the colorless nonripening (CNR) locus in tomato is a QTL. *CNR* encodes a SQUAMOSA promoter binding protein-like (SBP-box) transcription factor, which is methylated in the SBP-box promoter and repressed in the non-ripening strain [57•]. Similarly, epialleles have been found to associate with vitamin E accumulation in tomato [58], sex determination in melon [88], plant stature in rice [89], and mantled somaclonal variation in oil palm [90•]. Genome-wide studies investigating the methylome of diverse accessions of key crop species have indicated that the majority of these modifications are conserved within a species (see ref. in [91,92]) [93,94]. Between accessions, there are thousands of differentially methylated regions (DMRs), and 10–20% of these DMRs are negatively associated with gene expression. This suggests that these DMRs could influence phenotypes by altering gene expression.

In contrast to a perceived unstable nature of epimutations, some epimutations are stable and heritable in the progeny [95]. For example, DNA methylation mutation can create heritable epialleles, and epi-QTLs account for 60 to 90% of the heritability for two complex traits, flowering time and primary root length in *Arabidopsis* [55••]. Analysis of epigenetic recombinant inbred lines (epiRILs) in *A. thaliana* suggests that DNA methylation variation is associated with a large amount of heritable variation for ecological plant traits, including root allocation, drought tolerance, and nutrient assimilation, which could potentially contribute to morphological evolution [86,96,97].

Among 120 *A. thaliana* lines that are propagated by self-pollination, a significant amount of mutation accumulation (MA) is found by the 17th generation among some lines, while the distribution of these mutational effects on traits is rather symmetric, which argues against a common notion that mutations have predominantly negative effects on fitness traits [98]. A further study using two MA lines shows that while the spontaneously occurring epialleles are rare, nearly all (99.998%) methylated regions in the genome are heritable over selfing generations, half of which is associated with the methylation largely due to *cis*-acting effects, while the other half is related to *trans*-acting effects on methylation or demethylation and other possibilities [95]. Among ten different ecotypes over 30 generations of self-pollination, DNA methylation changes occur at a rate that is similar to that of DNA mutation, and the associated epialleles seem to be farther from transposable elements and less associated with short interfering small RNA expression [99•,100]. The stable inheritance of DNA methylation and their associated epialleles have an implication in plant evolution and a potential contribution to crop improvement [86,97,99•].

At the population level, although methylation variation can occur independent of genetic variation, thousands (2739) of methylation QTLs (mQTLs) have been identified in *Arabidopsis*, which are associated with 35% of the 3023 tested RdDM loci [101•]. Among these methylation loci, 12% overlap with genetic variation among different genotypes, suggesting genetic dependency of mQTLs. Moreover, the majority of targeted genes by RdDM are functional and their expression can change in response to environmental and developmental cues, including many known epialleles, such as *PAI* encoding phosphoribosyl anthranilate isomerase tryptophan biosynthesis, resulting in a fluorescent phenotype [102] and *Variation in Methylation1* (VIM1), a methylcytosine-binding protein required for centromeric heterochromatin [103]. Further analysis indicates epigenetic activation of many of these epialleles in pollen and seeds, suggesting a developmental role in the inheritance of epialleles [101•], probably through processes such as embryonic epigenetic reprogramming by transcription and chromatin factors [104].

Epigenetics regulation in polyploid evolution and domestication

Polyploidy is thought to facilitate crop domestication [105], through gain of domestication traits over evolutionary time scale [106] (Figure 2). A recent study on allotetraploid peanut (*Arachis*) using 26 anatomical, morphological, and physiological traits in six different events of hybridization and tetraploidization has shown that 19 traits, including plant stature, stomata and epidermal cells, and photosynthetic pigments, were transgressive in the allotetraploids relative to their diploid parents [107]. The data suggest that allotetraploidization (hybridity and/or tetraploidization) can enhance agronomic traits for cultivation. In sunflower, four FT paralogs generated from the WGD may exhibit different *cis*-acting or *trans*-acting effects on expression diversity, enabling the domesticated sunflowers to flower under long-day conditions, which coincide with the regions of QTLs of flowering under selection and domestication [108]. In hexaploid wheat, the Q gene, encoding an AP2-like transcription factor, is located in homoeologous group 5 chromosomes and controls several domestication-related traits, including free-threshing [109••]. Q allele in 5A (5AQ) is associated with domestication-related traits, while q alleles in 5D and 5B contribute directly and indirectly to the suppression of the speltoid (non free-threshing) phenotype. Thus, polyploidy-induced homoeologous alleles can control the harvesting trait during wheat domestication through transgressive expression of 5AQ, pseudogenization of 5Bq, and subfunctionalization of 5Dq.

A key question is: what causes expression differences of homoeologous loci that affect the traits subjected to selection and domestication? In *Arabidopsis*, natural variation of flowering time is largely controlled by two epistatically acting loci, namely *FRIGIDA* (*FRI*) and *FLOWERING LOCUS C* (*FLC*) [110]. *FRI* upregulates *FLC* expression that represses flowering [111,112]. Resynthesized *Arabidopsis* allotetraploids flower late, which consist of two sets of *A. thaliana* and *A. arenosa* *FLC* and *FRI* genes, respectively [34]. Late flowering is caused by upregulation of *A. thaliana* *FLC* (*AtFLC*) that is *trans*activated by *A. arenosa* *FRI* (*AaFRI*). *A. arenosa* has two functional *FLCs* (*AaFLC1* and *AaFLC2*) and a truncated *AaFCL3* [113]. The expression variation is associated with deletions in the promoter regions and first introns of *A. arenosa* *FLCs* and correlates with flowering time in the allotetraploids [34]. Natural *A. suecica* lines have retained strong *AtFLC* and *AaFLC* loci, leading to

extremely late flowering. Expression variation of *FLCs* correlates positively with histone H3K4 methylation and H3K9 acetylation and negatively with H3K9 methylation [34]. In another study of wheat *LEAFY HULL STERILE1* (*WLHS1*) gene, a homolog of rice *OsMADS1*, only the homoeolog in D subgenome (*WLHS1-D*) is expressed and functional in hexaploid wheat [38]. The *WLHS1* homoeolog in the A subgenome (*WLHS1-A*) has structural variation and no protein function, whereas the homoeolog in the B subgenome (*WLHS1-B*) is silenced by cytosine methylation. These data suggest mutually non-exclusively roles of chromatin modifications and sequence variation in expression and silencing of homoeologous loci, which could affect speciation and domestication traits like flowering time in allopolyploids.

At the genome-wide level, nonadditive gene expression is associated with *cis*-regulation and *trans*-regulation [114], as well as dosage-dependent and independent mechanisms [115]. Many dosage-dependent genes contribute to cell cycle, photosynthesis, and metabolism that are conserved across plant and animal kingdom, whereas dosage-independent genes are enriched in biotic and abiotic stress responses and plant-specific pathways. The dosage-dependent alleles are devoid of TEs and tend to correlate with H3K9ac, H3K4me3, and CG methylation, whereas the majority of dosage-independent alleles are enriched with TEs and correspond to H3K27me1, H3K27me3, and CHG methylation [115]. Compared with all genes, genes with only *cis* or only *trans* effects are enriched in the chromatin groups [114], which are associated with high levels of H3K9ac and H3K4me3 and different expression variance and histone mark distribution levels [40]. The genes with both *cis* and *trans* effects are underrepresented in the group with high levels of H3K27me3 and low levels of gene expression [114]. The genes with *cis* but not *trans* effects are associated with DNA methylation, which predominantly occurs at heterochromatin and transposons. Moreover, trans-chromosomal methylation changes are reported in *Arabidopsis* intraspecific hybrids [116].

These data collectively indicate a role for DNA methylation and chromatin modifications in gene expression and potentially phenotypic variation in plant polyploids (Figure 2). To test when and how these epigenetic changes or marks are established during evolution and domestication, Song *et al.* took the advantage of cotton genetics and evolution to investigate relationships among DNA methylation, epialleles, and phenotypic variation in wild and domesticated allotetraploid cottons, interspecific hybrids, and diploid ancestor-like species [36•]. Allotetraploid cotton was formed approximately 1–1.5 million years ago (MYA) [18] by interspecific hybridization between two diploid species [117], one having the A genome like in *Gossypium arboreum* (Ga, A₂) and *Gossypium herbaceum* (A₁), and the other resembling the D₅ genome found in extant species *Gossypium raimondii* (Gr); divergence of A-genome and D-genome ancestors is estimated at 6 MYA [117]. Five or more allotetraploids were derived from that individual polyploidization event, and subject to natural selection during evolution [118]. Domestication of cotton is predicted to take place approximately 5000 years ago [117]; two allotetraploid species, *G. hirsutum* L. and *G. barbadense* L. were independently domesticated into Upland or American and Pima or Egyptian cotton, respectively, for their higher fiber yield and wider geographical distribution [119]. The domestication characteristics were accompanied by many morphological changes

including loss of photoperiod sensitivity, reduction in seed dormancy, and conversion from tree-like wild species to an annual crop [119,120•].

The rate of differentially methylated cytosines, also known as single methylation polymorphism (SMP) [101•], among the conserved cytosines in *Gossypium* diploid and tetraploid species is much higher than that of nucleotide substitutions [36••], which may result in a greater number of rare alleles [101•]. However, the phylogenetic trees based on SMPs are similar to the ones based on nucleotide substitution rates, suggesting concerted evolution between nucleotide sequence and methylation changes [36••]. By comparing DMRs between A-genome and D-genome diploids, methylated cytosines are relatively stable and heritable. The results also suggest that the hybridization-induced DNA methylation changes are conserved during polyploid evolution and domestication. Between A and D subgenomes in the allotetraploid, there are homoeologous DNA methylation changes (hDMC), which correlate negatively with expression bias of the homoeologs, indicating an important role for methylation transfer between subgenomes in expression divergence between the homoeologs in allopolyploids [36••]. Furthermore, the changes in DNA methylation [36••], as well as histone modifications [35] between homoeologs could also contribute to asymmetrical evolution of A over D subgenomes in allotetraploid cotton [18].

Between two cultivated allotetraploids, *G. hirsutum* and *G. barbadense*, over 900 DMRs are conserved and associated with 519 genes, which are defined as epigenes or epialleles [36••]. One such epiallele is named cotton *CONSTAINS-LIKE2* homoeolog (*COL2*), which is a *CONSTAINS* (*CO*) homolog in *Arabidopsis*. *CO* controls photoperiodic flowering through the induction of *FLOWERING LOCUS T* (*FT*) and regulates *FT* expression via diurnal rhythms [121]. *COL2A* is hyper-methylated and silenced in all allotetraploids, while *COL2D* is also hypermethylated and silenced in wild allotetraploid cottons but expressed in cultivated allotetraploid cottons coincident with loss of DNA methylation [36••] reducing expression of *COL2D* by virus-induced gene silencing in cultivated cotton has delayed flowering and square formation for two weeks. These data indicate that loss of DNA methylation in the epiallele *COL2D* has resulted in *COL2D* expression, which changes the photoperiod sensitive wild *G. hirsutum* and *G. barbadense* species to photoperiod insensitive cultivated cottons. In crops, reduced or altered photoperiod response is one of the major ‘domestication syndromes’ [122]. Interestingly, in the hexaploid Persimmon (*Diospyros kaki*), differential methylation patterns of the sex determination gene *MeGI* are associated with developing male and female flowers with the higher DNA methylation levels in the *MeGI* promoter of the male flower buds [123]. The methylation of *MeGI* is dependent on small RNAs produced from the Y-encoded sex determinant pseudogene *OGI* [124]. We predict that many other candidate epialleles identified from allopolyploid cotton and other crops could shape morphological and physiological diversity during evolution and domestication. Furthermore, similar epigenetic changes in coordination with the genetic variation could lead to the evolution and domestication of complex traits in many polyploid and paleopolyploid crops.

Conclusions and future perspectives

Recent advances in sequencing technologies have made possible to generate a plethora of genomic and epigenomic resources, which have made a step closer to epigenetic engineering and breeding. An attractive aspect of epigenetic changes is stable but also reversible. One could use gene-editing technologies such as CRISPR/Cas9 to modify the epigenetic marks and reverse the epigenetic state. Alternatively, the existing epigenetic modifications such as methylation of stress responsive genes can be selected against in a breeding program. Some chemicals such as inhibitors for DNA methylation and histone modifications can also be used to induce novel epimutations for breeding and selection in crop plants. The observation that epigenetic changes induced by interspecific hybridization and polyploidization are stably maintained in allopolyploids suggests that perturbation of these modifications would release many new combinations of gene expression patterns related to phenotypic traits. Unleashing some of these traits in the selective sweeps of the cultivated crops would increase genetic and epigenetic diversity that can be used to improve crop production. Finally, comparative analysis of epigenomic data with genomic data such as genome-wide association studies would identify genetically dependent epialleles that can be used to effectively improve complex agronomic traits in crops, many of which are polyploids.

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Figure 1.

Formation of polyploid plants and nonadditive gene expression in allopolyploids. An autotetraploid (AAAA or BBBB) is formed by genome doubling from respective parents (AA or BB), while an allotetraploid (AABB) is produced by interspecific hybridization followed by genome doubling. Gene expression changes in an interspecific hybrid or allotetraploid can be additive or nonadditive (deviated from mid-parent value, MPV), suggesting an epigenetic cause. For simplicity, only one pair of chromosomes is used for each species.

Figure 2.

A model for epigenetic changes in interspecific hybrids, wild allopolyploids, and domesticated allopolyploids. Formation of interspecific hybrids or allopolyploids can be single origin like in *Gossypium* [117] or multiple origins like in *Tragopogon* [5], and with reciprocal genetic crosses (AB versus BA, by convention the maternal parent is listed first in a genetic cross) in some instances. Epigenetic marks such as DNA methylation are often associated with different kinds of transposable elements (TEs). During evolution and under natural selection, epigenetic changes such as DNA methylation that are induced in interspecific hybrids are largely maintained in wild allopolyploids, while gain or loss of epigenetic marks can occur. During domestication, most epigenetic marks are stably

maintained, while some new marks can arise or old epigenetic states may be reversed, in response to domestication process. The genes associated with these changes are defined as epialleles, which could play a role in the evolution and domestication of polyploid plants and crops. For simplicity, only DNA methylation marks are shown, and only two of the allotetraploids originating from a single hybridization event are shown in domesticated crops.

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Table 1

A partial list of DNA methylation and histone modifications on epigenetic regulation of gene expression

Modifications	Position	Enzymes Plants; mammals	Functions in transcription	References Plants; mammals
Histone methylation	H3K4me1(2,3)	ATX1/2, SDG2/8; SET1, SET7/9	Activation	[125,126]; [127]
	H3K9me2(3)	SUVH (H3K9me2); SUV39H1 (H3K9me3)	Silencing	[128,129]; [130]
	H3K27me3	CLF, MEA, SWN; EZH2	Silencing	[131,132]; [133]
	H3K36me2(3)	SDG8/26; NSD1,2,3, ASH1	Activation	[134]; [135]
Acetylation	H3K4, K9, K14, K18, K23, K27, and K79	HATs (GNAT, MYST, CBP, TAF); GCN5, MYST, p300/CBP, TAFII250	Activation	[136]; [137]
Histone variants	H3.1 H3.3	CENH3; CENP-A	Centromere organization	[138]; [139]
	H2A.Z H2A.W		Heterochromatin and silencing	[140,141]; [142]
DNA methylation	CG	MET1; Dnmt1	Silencing, activation, TE and centromere regulation	[47]; [143]
	CHG	CMT3; Dnmt3	Silencing, TE regulation	[144]; [145]
	CHH	DRM1/2, CMT2; Dnmt3	Silencing, TE regulation	[146]; [145]