



Genomic territories in inter-genomic hybrids: the winners and losers with hybrid fixation

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Abstract

Genomic technologies have enabled elucidation of spatial organization of genomes and gene expression in the nucleus of the homoploid hybrids and allopolyploids. It has been shown that the participating genomes in the inter-genomic hybrid occupy definite territories in the combined nucleus forming concentric rings. The spatial position of the partner genomes is largely dependent on the relative size of their chromosomes and centromeres. In terms of genetic expression, the inter-genomic hybrids do not truly represent the combination of parental genomes, instead, there is sub-genomic dominance of one genome over the other in accordance with predisposed nucleotype. Generally, the genome with larger chromosomes surrounds the sister genome in the stable hybrid, but the genome destined to be eliminated in the unstable hybrid lie in the peripheral zone of the hybrid nucleus. The peripheral genome tends to express preferentially, but there is repression of gene expression in the surrounded genome owing to enhanced methylation / reduced transcription, making them winner or loser respectively. In a battle between the parental genomes in the unstable hybrid, the inter-genomic dosage between the participating genomes, as well as, diminution or loss of centromeric histones in the losing genome adversely affects kinetochore-microtubule assembly. The latter leads to uniparental elimination of such genome in the wide hybrids during developmental phase.

Keywords Inter-genomic hybrid · Spatial genomic organization · Genomic territories · Subgenomic dominance · Winners and losers in hybrid fixation

Introduction

In plants where asexual reproduction is obligatory or callus cultures where cells get open opportunity to proliferate, there are increased chances of de novo formation of heterogeneous collection of cells owing to enhanced mitotic errors. Such a behaviour is considered an important resource to realize variation even with somatic division enabling speciation in asexually propagated species [34], and evolutionary fitness of balanced genomes through passage of morphogenetic sieve [20]. In a homoploid hybrid or allopolyploid, the union of multiple genomes within one nucleus may require

new spatial arrangement of the progenitor genomes in the inter-genomic reconstitution. In the hybrid nucleotype one genome may affect the gene expression of the other [16]. Also, there may be partial or complete loss of chromosomes of one parent during developmental stabilization [12, 14, 21, 29]. Thus, the obvious question that follows is about the winners and losers in search of selection for fitness and stability in a wide hybrid. At individual cell or chromosome level it seems difficult to draw direct inferences, but could be possible if we consider whole genomes in the inter-genomic hybrids through large scale understanding of genomic territories, inter-genomic organization and character expression.

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Genomic territories in inter-specific hybrids

A good number of studies have been performed on natural and synthetic inter-genomic hybrids with respect to physical positioning of the participating genomes in the hybrid nucleotype. Leitch et al. [22], based on their study undertaken on sectioned material of the manmade hybrid between *Hordeum*

vulgare × *Secale africanum* deduced that the two genomes, contributed by different parents, tend to be spatially separated at interphase, prophase, as well as at metaphase in the wide hybrid. GISH based analysis that categorically differentiated the two genomes, further revealed that the genome originating from *H. vulgare* tended to be located more centrally than that from *S. africanum*. In another hybrid between *Hordeum vulgare* × *H. bulbosum*, the *H. bulbosum* chromosomes were found to be located in outer periphery [33]. Similar situation about spatial disposition of ancestral genomes have been observed in the naturally occurring allopolyploid wild grass *Milium montianum*, where the two ancestral genomes exhibited tendency to lay apart, where M genome with small chromosomes was found to be surrounded by V genome with larger chromosomes [3].

An exhaustive analysis undertaken in genomic disposition on tetraploid cotton, *Gossypium hirsutum*, AADD (i.e. A genome of *G. arboreum* and D genome of *G. thurberi*) and synthesized tetraploid cotton, AAGG (i.e. A genome of *G. arboreum* and G genome of *G. bickii*), Han et al. [15] demonstrated that the two sub-genomes were separated in a radial pattern where small genome (D or G) tended to concentrate in center and the large genome (A) scattered

along the periphery. This established that the subgenomes in the inter-specific hybrid conform to spatial genomic territory, where the genome with larger chromosome occupies peripheral territory (Fig. 1a, b). Similar pattern of spatial genomic disposition was observed in the somatic hybrids of *Nicotiana* × *Atropa*, where the genome of *A. belladonna* with small chromosomes tended to lie at the center of the metaphase plate whereas the large chromosomes of *N. chinensis* were scattered along the periphery [13].

In a recent study on the spatial nucleus architecture in various wheat × rye and wheat × barley introgression lines it has been shown that the introgressed chromosome /chromosome arm tend to occupy discrete, separate positions in different somatic tissues during different cell cycle stages. It is further suggested that there is apparent link between the length of chromosome and spatial positioning, wherein shorter chromosomes or chromosome arms are preferentially located closer to the center of the nucleus and the longer chromosomes and chromosome arms occupy more peripheral areas of the nucleus [18].

However, in the interspecific hybrids that exhibited tendency of uniparental elimination, whether partial or complete, the genome of the parent that was destined to be

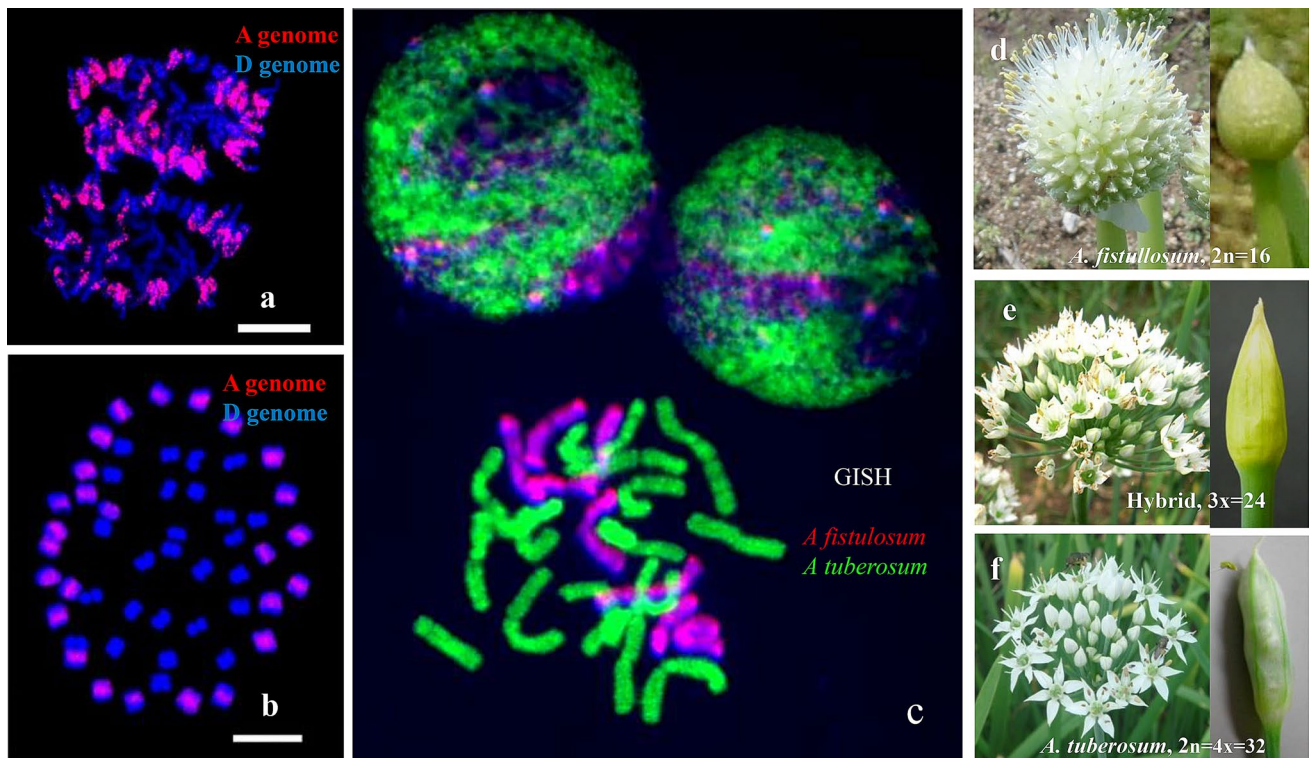


Fig. 1 GISH based genomic differentiation and their spatial orientation in the nucleus. **a, b** *Gossypium* hybrid—showing genomic territories at anaphase and metaphase of A (peripheral) and D (central) genome; **c** *Allium* hybrid—showing genomic territories at interphase and metaphase wherein *A. tuberosum* is peripheral and *A. fistulo-*

sum is towards centre, **d–f** Inflorescence and bud of the parent (**d, f**) and hybrid (**e**)—hybrid ‘e’ shows more resemblance towards parent ‘f’ that show peripheral localization in the hybrid nucleus (**c**). Figure source: a, b [15], and c–f [40]

eliminated was found to occupy peripheral position irrespective of the chromosome size. This is apparent from the observations made on the interspecific hybrids between oat \times maize and wheat \times pearl millet, wherein the introgressed chromatin was predominantly located at the nuclear periphery. GISH based localization of maize chromosomes in oat \times maize addition lines further showed that the added maize chromosomes are preferentially positioned at the nuclear periphery [1]. The peripheral positioning of pearl millet chromatin was shown to be part of a chromosome elimination process that involved the formation of nuclear extrusions in the interphase [12]. This is in line with spatial disposition of the two genomes in the *Hordeum vulgare* and *H. bulbosum* hybrids, where the *H. bulbosum* chromatin destined for elimination is deposited at the nuclear edge [17].

From the above it becomes clear that the participating genomes are spatially organized in the nucleus at genome level, and there is apparent link between the chromosome size and behaviour during development that shape the nuclear architecture in the hybrid.

Winners and losers in the spatial organization

Correlation of phenotype with chromosome position

It has been observed in many interspecific hybrids that they do not reflect mid-parent appearance of the parental species, instead exhibit a form of parental dominance of one species over the other owing to different gene expression properties [1, 14]. Finch and Bennett [10] reported that the F1 hybrid between *H. vulgare* \times *S. africanum* does not exhibit intermediate appearance of the two parents, but show resemblance with the peripherally located *Secale* parent for many different characters. Similarly in Triticale (a hybrid between wheat, *Triticum durum* \times rye *Secale cereale*) it was observed that the hybrid does not resemble its true intermediate, but show many more features of rye, parent that has peripheral disposition. The observations suggest that in the hybrids the peripheral genome tends to be expressed preferentially [16]. Similar situation was observed in *Allium* hybrid (*A. fistulosum*, $2n = 16 \times A. tuberosum$, $2n = 32$), wherein hybrid exhibited more resemblance to peripherally located genome of *A. tuberosum* (Fig. 1c–f) [40]. Further, in all these instances the genome with larger chromosomes was found to be preferably positioned towards periphery in the hybrid nucleus.

The subgenomic dominance

(a) **Gene Expression** It is a common observation that during the course of intergenomic hybrids fixation, one of the

parental genome becomes dominant over the other, a phenomenon called subgenomic dominance. At the same time, as pointed above the physical positioning of the chromosomes and genomes in the hybrid nucleotype influences genomic imprinting of one genome over the other, wherein the peripheral genome is found to exhibit subgenomic dominance in phenotypic expression. One simple explanation that could be given is that the masking effect of peripheral genome reduces the transcription factor accessibility associated with chromatin remodelling [23]. Other factor attributed to reduced gene expression in the submissive genome is methylated TEs that reduce / silence the expression in nearby gene [1, 4, 14, 30]. This is consistent with an earlier observation whereby treatment with the demethylation agent azacytidine was found to release hidden variation in triticale hybrid which was lost because of genomic imprinting phenomena [16].

(b) **Gene fractionation and centromere dysfunction** In order to obtain a more diploid-like state, polyploid genomes will undergo gene loss (biased fractionation) [1, 8, 24, 39], DNA purging [35] and genome downsizing [14]. Furthermore, it was shown that the dominant subgenome, which retains more genes, also exhibits significantly higher overall gene expression compared to the submissive subgenome [1, 32]. As such, the less fractionated and more highly expressed subgenome is referred to as the ‘dominant subgenome’ and the more fractionated and lowly expressed subgenome is referred to as the ‘submissive subgenome’. Collectively this phenomena is called ‘subgenome dominance’ [1]. In addition to just gene fractionation, in certain artificial intergenomic hybrids subgenomic dominance has been observed to the extent that the submissive subgenome is eliminated all together owing to centromere dysfunction [31].

In this respect it is worth mentioning the observations made on the structural organization of chromosomes and centromeres of the participating genomes in the interspecific hybrids between *Hordeum vulgare* \times *H. bulbosum*, where both stable or unstable hybrids (showing gradual elimination of *bulbosum* chromosomes) are known to be formed depending upon genotype of the *bulbosum* parent and temperature of cultural environment during embryo development [2, 11]. Schwarzacher et al. [33] while reconstructing the three dimensional position of the chromosomes and centromeres in root-tip and premeiotic mitosis of the said hybrids have shown that centromeres of the parental genomes tend to lie in spatially separated domains in both tissues. Whereas, there is apparently no difference in the mean chromosome size of the two genomes, but the *H. bulbosum* chromosomes appear less condensed with weaker (or smaller) centromere-associated structures compared to *H. vulgare* genome with larger centromere and more condensed chromosomes. It is further observed that *vulgare* genome is disposed in the central zone and the *bulbosum* genome is more peripheral in

the nucleotype. It was therefore suggested that the activity, rate or timing of production of the centromeric structures is likely to be under genetic control, and might be correlated with the tendency of chromosomes of particular genome to be lost in unstable hybrids [33].

(c) In the battle between parental chromosomes in the intergenomic hybrids—the centromeres hold the key: One of the important resource to understand genomic winner or loser i.e. battle between parental chromosomes in the inter-genomic hybrids is the classic example of artificial hybrids between *Hordeum vulgare* × *H. bulbosum* [6]. Depending upon the genotype and gamete source of *bulbosum* parent, both stable and unstable hybrids could be produced. Also culture conditions with respect to temperature and nutrition during embryo rescue could help realize stability to the otherwise unstable hybrid to some extent through regulation of the cell cycle [11].

In order to elucidate the reason and mechanism behind differential behaviour of the partner genomes in the intergenomic hybrids, Sanei [31] studied the structural organization of centromeres of the stable vs unstable hybrids of *H. vulgare* × *H. bulbosum* through immunolocalization. It has been found that in the interspecific hybrids of barley the uniparental chromosome elimination is preceded by the loss of a histone H3 variant known as the centromere-specific histone H3 variant (CENH3). The CENH3 deficiency in the *H. bulbosum* turns its centromere inactive for attachment to the spindle required for regulated chromosome segregation. This triggers uniparental elimination of *bulbosum* chromosomes in the unstable hybrid. Such centromere inactivity results from centromeric loss of CENH3 rather than uniparental silencing of CENH3 genes [31].

The elimination of the *H. bulbosum* genome in unstable hybrids is gradual, taking place over several days after pollination [2, 9]. When chromosomes are replicated during S phase of the cell cycle, histones including CENH3 are distributed between the two sister chromatids [7]. These observations suggest that *H. bulbosum* chromosomes enter the zygote with a normal complement of CENH3, which is gradually depleted by several rounds of DNA replication until the kinetochore is no longer able to function. Therefore, reloading of CENH3 after DNA replication is specifically defective in *H. bulbosum* derived chromosomes, although it is normal in chromosomes from the *H. vulgare* parent [6].

Wang and Dawe [37], based on analysis of a large number of wide crosses, including oat, barley, and wheat (large centromere species) with sorghum, maize, pearl millet, adlay millet, and perennial ryegrass (small-centromere species), where genome elimination has been attributed to centromere size dimorphism, have proposed a centromere size model that suggests that centromere size has bearing on haploid production, as visible from failure in centromere function in the lines with small / weak centromere. Centromeres with

defective or mutated CENH3 have a lower loading capacity and sport smaller centromeres, resulting in chromosome loss of the small-centromere parent in the intergenomic hybrid.

That the defective centromeres are lost in centromere-mediated haploid production have been experimentally demonstrated by Ravi and Chan [27]. Using a modified version of CENH3 called “tailswap-CENH3” they were able to induce haploids at a very high frequency (25–45%) in the *Arabidopsis* null mutant on account of non-functional centromeres (thus inactivating chromosome movement) of the tailswap parent that are eliminated. In fact the CENH3 mediated centromere manipulation has emerged as a powerful tool for uniparental chromosome elimination to realize haploid production for plant breeding applications [5, 28, 38].

(d) Uniparental chromosome elimination and intergenomic balance: As mentioned above, the primary reason for selective elimination of a given genome during embryonic development in wide hybrids is on account of centromere dysfunction. But equally important is the spatial orientation of the participating genomes in the hybrid nucleus. It is observed that the genome destined to be eliminated is positioned in peripheral territory owing to weaker centromere function, slow condensation and shorter chromosomes to some extent [19, 21, 25, 31]. Further, in the intergenomic hybrids where phenomenon of selective chromosomal elimination is widespread, e.g. in *Hordeum*, it is the ratio of the parental genomes in the hybrid combination that determines whether predominantly haploid or hybrid progeny are produced, and which genome is more likely to be eliminated, e.g. in a hybrid between tetraploid and diploid species of *Hordeum*, it is the diploid genome that would be eliminated as reported for several species of *Hordeum* [36]. Also, there is a hierarchy of species dominance in chromosome elimination [36]. Mukai et al. [26] further confirmed this assumption by demonstrating that the D-genome plays a critical role in the formation of haploid *Aegilops tauschii* through *Imperata cylindrica* mediated uniparental chromosome elimination.

Concluding Remarks: It could be conceptualized that in intergenomic hybrids, the partner genomes owe predisposed spatial territories; wherein peripheral genome incur sub-genomic dominance, but prone to uniparental elimination owing centromere dysfunction. So what have we learned from the understanding of spatial orientation of genomes in the context of its implications in hybrid fixation and generation of new genomic states? Fixation of wide hybrids while maintaining the genomic territories of partner genomes also requires inter-genomic compatibility for coordinated cell division / kinetochore functionality, as well as minor readjustments in the genetic material through gene fractionation and gene expression. But in the incompatible hybrids one dominant genome could eliminate the other through

inactivated centromeres of the latter. Such findings have enabled the development of haploid production technology through wide hybridization for its utilization in crop breeding programmes. Further, the observation that centromere dysfunction could result into chromosome elimination per se, has led to the development of technical advances for creating haploids at will through artificial manipulation of centromere function of one of the parents for its auto-elimination during embryonic development, leaving only the haploids of choice at the end. This has opened a new era of development in plant breeding.

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Conflict of interest Authors declare no conflict of interest.

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