Revising the selfish DNA hypothesis
new evidence on accumulation of transposable elements in heterochromatin

The bulk of the eukaryotic genome is composed of families of repetitive sequences that are genetically silent and exhibit various types of instability. Transposable elements (TEs) are particularly commmon in heterochromatic regions of the genome – a location where TEs might do less damage to their host. Recent advances suggest that the relationship between TEs and heterochromatin might not be quite so straightforward.

Transposable elements represent a conspicuous fraction of the eukaryotic genome (12% in *Drosophila* and 35% in humans)[1] whose long-term evolutionary significance remains elusive after almost two decades of intensive experimental work and theoretical modelling. The questions being asked are whether ubiquity and persistence of TEs in evolution rest primarily on their replicative advantage over the host genome or on the contributions they make to the genetic plasticity and evolution of their hosts[2,3].

One of the testable parameters in this matter is the genomic distribution of TEs: random insertion and lack of fixed elements are consistent with the view of TEs as selfish DNA, whereas specificity of insertion and fixed elements might reflect functional interactions with host genes. There is evidence for elements, or DNA segments still recognizable as parts of TEs, that underwent fixation probably under selective pressure for regulatory roles[4]. In addition, although TEs can insert into many different locations, they often display some selectivity for genomic targets that may be defined by a variety of parameters such as chromatin accessibility, DNA sequence, protein–DNA and protein–protein interactions and bent DNA (Ref. 5).

TEs as components of heterochromatin

Heterochromatin represents another conspicuous fraction of the eukaryotic genome (of the order of 15% in humans and 30% in *Drosophila*)[6] composed primarily of a variety of repetitive sequences, most notably satellite DNAs. There is a growing evidence in evolutionarily distant organisms for a build up of TEs in this genomic region (Table 1). Perhaps the best documented example is in *D. melanogaster* where TEs form prominent clusters within heterochromatin at locations that are distinctive of different families, and are stable in unrelated stocks[7]. In Syrian hamster, over half of the genomic *IAP* elements are accumulated in heterochromatin, including the entire *Y* chromosome[8]. In maize, retroelements are especially abundant in heterochromatic knob regions[9]. Hence, TEs appear as common, often conspicuous components of heterochromatin in eukaryotes.

Deleterious effects in euchromatin versus targeting of heterochromatin

Under the selfish DNA hypothesis, elements would accumulate in heterochromatin because there are fewer genes there, that is, inserted elements are less likely to be deleterious. Under the same hypothesis, another interpretation envisages a chain of events beginning with transposition and ending with accumulation in heterochromatin[2]. The first step is transposition and the ensuing increase of the copy number of elements. Such increase enhances the probability of meiotic recombination at non-homologous sites (ectopic recombination), which produces gross chromosomal rearrangements giving rise to aneuploid gametes. Upon selection against such rearrangements, TEs are expected to be overabundant in heterochromatin where recombination is strongly reduced compared with euchromatin. Under both interpretations build up in heterochromatin would be due to selection against deleterious effects in euchromatin brought about by instability of TEs.

This has been tested in *D. melanogaster* by asking whether there are transposon families that are more unstable than others (possibly encoding more active reverse transcriptases or transposases) and, if so, whether those elements are more abundant in heterochromatin than others. It turns out that there are no families inherently more unstable than others. This was shown by the finding that the hierarchy of instability between the same families differs among stocks (for an overview see Ref. 10). By contrast, the fraction of elements located in heterochromatin differs between transposon families and is by and large maintained in unrelated *D. melanogaster* stocks[7,11,12]. Thus, accumulation in heterochromatin does not appear to be the direct outcome of instability.

In addition, accumulation in heterochromatin does not seem to be related to intrinsic properties of transposon families because the same elements may be abundant in *D. melanogaster* and not in the sibling species *D. simulans* suggesting that this trait is determined by some sort of interaction between each transposon family and the host genome[13].

Together, these results do not support the view of the deleterious effects of TEs in euchromatin, brought about directly at insertion sites or indirectly through ectopic recombination, as the primary reason for accumulation in heterochromatin. Consistent with this conclusion is recent evidence about the dynamics of such accumulation. In *D. melanogaster*, *de novo* transposition of *I* elements very efficiently generates mutation of single-copy heterochromatic genes. The overall frequency of lethal mutations mapping to 13 loci located in the proximal heterochromatin of chromosome 2 approaches 10^{-2}, a value about one order of magnitude higher than the mutability of euchromatic genes located on the same chromosome[14]. Another case of *de novo* targeting of heterochromatin has been described in an interspecific wallaby hybrid where massive amplification of retroelements occurs in pericentromeric regions upon

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TABLE 1. TEs in the heterochromatin of animals and plants

Species	Transposon	Location within heterochromatin	Ref.
D. melanogaster	*copia, gypsy, 1731, blood, mdg1, I, F, Doc*	X, Y, 2, 3	7
	G	X	7
	Het-A, TART	Telomeres, Y chromosome	17
	P	Y[a]	7
	hobo	X, 2, 3[b]	7
D. simulans	*copia, mdg1, gypsy*	Y chromosome and elsewhere	13
D. miranda	*TRIM, TRAM*	Neo-Y chromosome	20
Syrian hamster	*IAP*	Y chromosome and elsewhere	8
Maize	*grande*	Knob of chromosome 9	9
Allium cepa	*Ty1-copia*	Telomeric heterochromatin	24
A. thaliana	*Ty1-copia*-like	Paracentromeric heterochromatin	25
Cicer arietinum	*Ty1-copia*-like	Paracentromeric heterochromatin	25

[a]Only detected in the strain Fairfield-2.
[b]Polymorphic for the presence among the strains.

instability triggered by demethylation[15]. Hence, accumulation might be a rapid process as opposed to long-term selection against euchromatic inserts, and heterochromatin appears as a preferential target rather than a safe haven where TEs would be shielded from selection against the damage they cause. The determinants of such regional specificity are unknown but it has been suggested that it may result from high density in heterochromatin of DNA nicks that might be repaired by TEs (Refs 1, 16).

A role for TEs in heterochromatin: promising hints

Once in heterochromatin, elements might acquire a role and become subject to positive selection. In *D. melanogaster* *HeT-A* and *TART* elements maintain the integrity of chromosomal ends (telomeres)[17]. Transcripts of TEs in heterochromatin might have a role in the repression of transposition in somatic cells and in the function of *Drosophila* fertility genes (for an overview see Ref. 16). Regulatory sequences of TEs might become a functional part of heterochromatic genes, similar to documented cases of this kind in euchromatin[3,4]. Conservation of the distribution patterns of different TE families within heterochromatin of *D. melanogaster* is consistent with a structural and/or functional role[7]. In maize, retroelements appear as structural components of all centromeres[18] and might contribute to the genetic effects associated with the knob heterochromatic regions[9].

There is also evidence for a contribution of TEs in the evolution of heterochromatin. Tandem arrays of engineered *P elements* give rise to *de novo* formation of heterochromatic-like structures[19] whereas 5S genes do not. Thus, formation of heterochromatin seems to have some sort of sequence requirement which is met by at least some TEs. Consistent with this conclusion is the massive insertion of *TRIM*, *TRAM* and *NY* retroelements that has been correlated with heterochromatinization of the neo-Y chromosome of *D. miranda*[20].

The ability of TEs in promoting chromosomal rearrangements of euchromatic regions is well documented[21]. Now, evidence from *D. melanogaster* and wallaby shows that retroelements might reshape heterochromatin as well by causing deletions, inversions and amplifications[14,15]. This suggests that the inherent instability of TEs contributes to the changes in amount and distribution of heterochromatin that characterize the evolution of animals and plants[6]. Heterochromatic regions are known to harbor active genes and to be involved in structural functions, such as centromeric activity and chromosome pairing[22,23]. Restructuring of these regions might give rise to variants that could establish a fertility barrier that promotes evolutionary divergence and speciation.

Conclusions

Here we draw attention to recent evidence about accumulation of transposable elements in heterochromatin. The dynamics of such accumulation, the specificities in targeting and location of different families and roles they might acquire within heterochromatin is at variance with the view of elements being abundant in this region because of the damage they cause in euchromatin. Rather than mere addition of 'junk DNA' to the genomic 'wasteland', accumulation of TEs in heterochromatin might turn out to be an aspect of a relevant evolutionary interaction between these two ubiquitous and fluid components of the eukaryotic genome.

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