Trends in Ecology & Evolution

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Opinion

Adaptation to Global Change: A Transposable Element–Epigenetics Perspective

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Understanding how organisms cope with global change is a major scientific challenge. The molecular pathways underlying rapid adaptive phenotypic responses to global change remain poorly understood. Here, in this context, we highlight the relevance of two environment-sensitive molecular elements: transposable elements (TEs) and epigenetic components (ECs). We first outline the sensitivity of these elements to global change stressors and review how they interact with each other. We then propose an integrative molecular engine coupling TEs and ECs and allowing organisms to fine-tune phenotypes in a real-time fashion, adjust the production of phenotypic and genetic variation, and produce heritable phenotypes with different levels of transmission fidelity. We finally discuss the implications of this molecular engine in the context of global change.

A Molecular View of Responses to Global Change

Understanding the molecular mechanisms underpinning phenotypic responses of organisms to stress is central to evolutionary biology [1,2]. In the last decades, major advances have been made in this field, notably by highlighting several environment-sensitive molecular elements potentially guiding and accelerating phenotypic and genetic responses to stress [3]. These elements include ECs and TEs.

ECs constitute a molecular network (Box 1) that can adjust phenotypes instantaneously (i.e., during development) and/or generate new phenotypes – sometimes transmitted across generations – without modifying the DNA sequence [4]. They strongly connect the surrounding environment with the genome and the phenotype, hence playing a central role in organisms' response to stress [5,6]. TEs are stretches of DNA sequences that can move and amplify their copy number within a host genome [7]. Their activity can be triggered by environmental cues, accelerate mutation rates, and rewire regulatory networks (Box 2) [8,9]. As first claimed by Barbara McClintock [10], TEs constitute a significant adaptive response of the genome to (unanticipated) environmental challenges. Interestingly, TEs and ECs are intimately linked, potentially amplifying their actions on phenotypes and genotypes [11–14].

While TEs and epigenetics are increasingly acknowledged as main actors of organisms' phenotypic responses to various stressors [5,6,15,16], their combined actions in promoting such responses have rarely been considered explicitly in the context of **global change** (see Glossary) (but see [12,13]). Although apparently slow at the human scale, global change is fast and drastic at the evolutionary scale, affecting most living species and initiating the ongoing sixth

Trends

A major recent observation is that populations can rapidly and lastingly adapt to global change.

Understanding the molecular pathways underpinning rapid phenotypic responses to global change is central to evolutionary and conservation biology.

Epigenetic components (ECs) and transposable elements (TEs) are environment-sensitive molecular mechanisms enabling organisms to rapidly cope with environmental stressors in the short and long term.

ECs and TEs strongly interact with each other, hence constituting an environment-sensitive molecular engine rapidly producing new phenotypes and genotypes in response to stress.

This TE–EC engine represents an overlooked molecular engine of rapid adaptation to global change.

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mass extinction [17]. Recent observations, however, showed that adaptive phenotypic responses of populations to global change can be extremely rapid [2,18]. This recurrent observation was surprising because the pace of evolutionary responses is predicted to be not rapid enough to cope with the current rate of environmental change [19]. This has renewed interest in the evolutionary role of **phenotypic plasticity** [20] and promoted the idea that evolution by natural selection regularly unfolds over (short) ecological timescales (i.e., **micro-evolution**) [18,21]. More recently, fundamental questions were raised concerning the molecular mechanisms allowing organisms to react so rapidly (and adaptively) to these drastic environmental changes [22].

Here we argue that TEs and ECs might jointly constitute a powerful molecular engine triggering rapid adaptive phenotypic responses to global change. We first review evidence that TEs and ECs are sensitive to environmental stressors related to global change and that these activities can promote rapid phenotypic and genetic changes in organisms. We then describe how TEs and ECs mechanistically interact with each other to form a complex molecular network. We build on these findings to propose that TEs and ECs can be integrated into a single mechanistic engine potentially permitting organisms to rapidly and lastingly cope with global change. We finally suggest research avenues to incorporate this engine into the reasoning of evolutionary ecologists concerned with global change.

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Box 1. The Most Common ECs that Promote Phenotypic and Genetic Variations (Figure I)

DNA Methylation

DNA methylation, the addition of a methyl radical to a DNA nucleotide, modifies the accessibility of DNA to binding proteins (e.g., transcription factors) hence modifying (most often inhibiting) gene expression [71]. When occurring in the germline, some patterns of DNA methylation, usually thought to be reset during meiosis, nonetheless persist across generations leading to heritable phenotypic changes [41]. Although less acknowledged, DNA methylation is also mutagenic as it favors deamination leading to C-to-T transitions [58] and can locally affect meiotic recombination rates [72]. Thus, as for TEs, DNA methylation also has the potential to lastingly affect the genome architecture.

Histone Modifications

Histones are central molecules in chromatin formation [73]. Post-translational modifications of histone tails (about 100 types are identified) can alter the affinity of histone complexes for DNA, thereby changing the spatial configuration of chromatin and affecting the accessibility of DNA sequences to transcription enzymes, ultimately affecting gene expression [73]. Some of these histone tail modifications are heritable over several generations and are associated with changes in key life-history traits [63].

Noncoding RNAs

Recent advances in transcriptomics revealed an amazing diversity of non-protein-coding RNAs (i.e., ncRNAs) participating in the transcriptional and post-transcriptional control of gene expression [74]. As such, many ncRNAs are integral parts of the epigenetic regulatory network [74]. Some functional ncRNAs are transmitted across generations through the nourishing tissues of parental gametes, providing another source of nongenetic inheritance [75].

Intricate Epigenetic Cross-talk

DNA methylation and histone tail modifications can interact through their respective enzymatic machinery, hence reinforcing their phenotypic influence [76,77]. DNA methylation can dictate histone tail modifications [76] by guiding the reproduction of histone-based chromatin spatial conformation after DNA replication. Conversely, the establishment of DNA methylation during early development can be mediated through modifications at histone tails [76]. Moreover, some ncRNAs partly control *de novo* DNA methylation and histone tail modifications [74]. In particular, they contribute to the reestablishment of epigenetic patterns after meiosis and are thus likely to be involved in the fidelity of some epigenetic patterns across generations [41].

The synergy between these mechanisms constitutes a self-reinforcing and self-perpetuating cycle of epigenetics leading to long-term transcriptional repression [74,76,77]. As a result, epigenetic regulations not only modulate gene expression but also ensure the fidelity of gene expression states over generations [76].

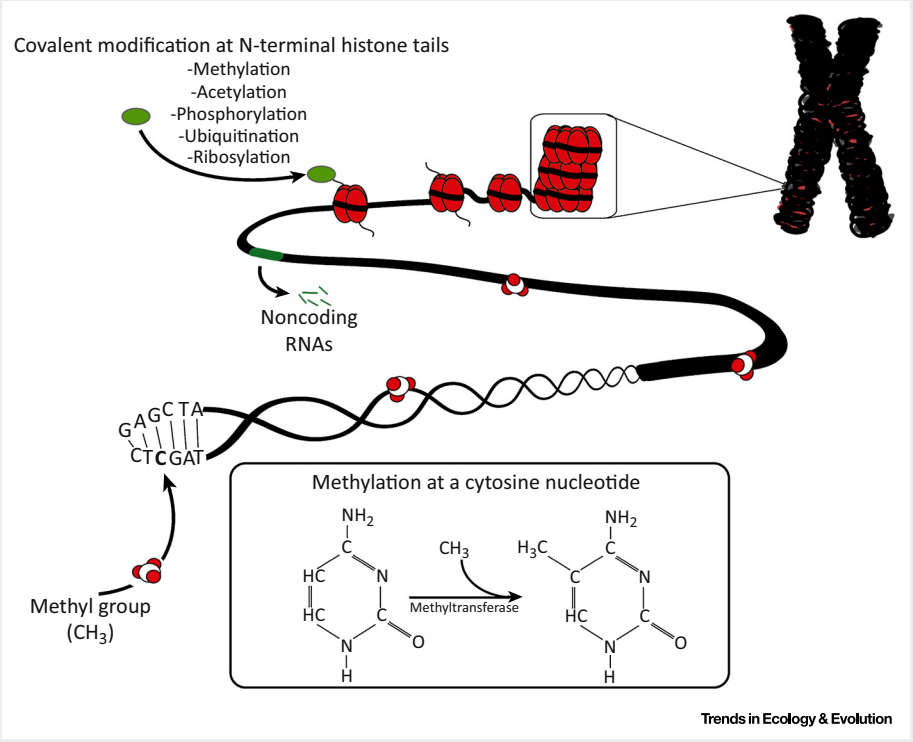


Figure I. Illustration of the Most Common Epigenetic Components that Promote Phenotypic and Genteic Variations.

TEs and ECs as Environment-Sensitive Sources of Phenotypic and Genetic Variants

TEs and ECs Are Sensitive to Global Change Stressors

TE activity can be modulated by many biotic and abiotic environmental factors, in some cases through the cooption of regulatory responses from the host [16,23]. In particular, stressors related to global change can trigger TE activities in fungi, plants, and animals [16,24,25]. For instance, exposure to both UV light and cold stress induce the mobility of the *OPHIO2* transposon in the fungus *Ophiostoma novo-ulmi*, the causal agent of Dutch elm disease [24]. Similarly, heat stress increases the expression and mobilization of *mariner-Mos1* in *Drosophila simulans* [26].

Epigenetics are also sensitive to global change stressors such as drought, warming, and pollutants [6,27]. For instance, global DNA methylation levels in human blood cells are modified after exposure to traffic carbon particles [28]. Furthermore, heat stress induces genome-wide modifications of methylation patterns in the grass *Leymus chinensis* [29]. Field evidence also largely suggests that environmental conditions affect the **epigenomes** in wild populations [30]. For instance, invasive populations of Japanese knotweed (*Fallopia japonica*) established in various habitats in northeastern America display massive epigenetic differentiation – largely exceeding the observed genetic differentiation – and some of the epigenetic patterns might respond to local habitat conditions [30].

By activating TEs and epigenetics, global change stressors are turning on molecular machineries that might have profound consequences on the phenotypes of organisms, a fact that we review hereafter.

Glossary

Alternative mRNA splicing: biological mechanism by which combinations of gene introns are spliced and gene exons are assembled to form different protein isoforms from a single gene. Alternative mRNA splicing is a major mechanism of transcriptome diversity and phenotypic plasticity.
Epigenome: arrangement and distribution of epigenetic patterns at the whole-genome level.
Global change: encompasses all forms of environmental change observed at the global scale during the past two centuries and thought to be mainly due to human activity. Environmental changes associated with global change include climate change, pollution, ocean acidification, overexploitation of natural resources, crop engineering, habitat fragmentation, biological invasions, and emerging diseases.
Microevolution: evolutionary changes that occur within species or populations at contemporary ecological scale (i.e., over a few generations).
Phenotypic canalization: process by which the phenotypic expression of genetic variation is reduced.
Phenotypic plasticity: ability of an individual genotype to express different values of a given phenotypic trait in different environmental conditions. This term also includes the particular case of transgenerational plasticity, which describes the ability of an individual genotype to produce different offspring in different environmental conditions.
Retrogene: DNA gene copied back from RNA by reverse transcription.
Transduplication: process by which a gene or a fragment of a gene is incorporated into a TE and duplicated and transposed as the TE moves throughout the genome.

Box 2. Mechanisms by which TEs Generate Genetic and Phenotypic Variation

TEs as Generators of Genetic Diversity

The frequent mobility of TEs can accelerate mutation rates (Figure IA). For instance, the activity of the element *Tol2* in laboratory strains of the medaka fish is responsible for a 1000-fold increase in mutation rate in a pigmentation gene, reaching up to 2% per gamete [78], often leading to new heritable phenotypes such as albino-like individuals [78]. TEs can also induce gene conversion and both homologous and nonhomologous recombination [15].

Alternatively, several mechanisms have been identified by which TEs can build on preexisting genetic support to generate genetic variants from which functional evolutionary novelties can emerge [25]: insertion of new exons (Figure IB, yellow box) into genes (i.e., exonization); aggregation of fragments of distinct genes (Figure IC, colored boxes) within the same TE; and retrotranscription of gene mRNAs and insertion of the resulting **retrogene** (Figure ID, colored boxes represent exons) in the genome.

TEs as Modulators of Gene Expression

TEs can affect gene expression quantitatively when inserted into a coding region or into promoter regions, as spontaneous genetic mutations do (Figure IE). Alternatively, TEs can carry regulatory sequences in their promoter regions. New TE insertions can thus modify gene expression in response to stress to which the elements are themselves responsive (Figure IF). **Transduplication** can also result in the duplication and transposition of a newly integrated gene as part of the TE, which generally enhances the phenotypes encoded by this gene (Figure IG) [79].

Finally, TEs can modulate gene expression qualitatively. TEs can modify **alternative mRNA splicing** by introducing internal splice-site-like structures and/or polyadenylation signals into genes, contributing to the broadening of transcript diversity from a single gene [80] (Figure IH).

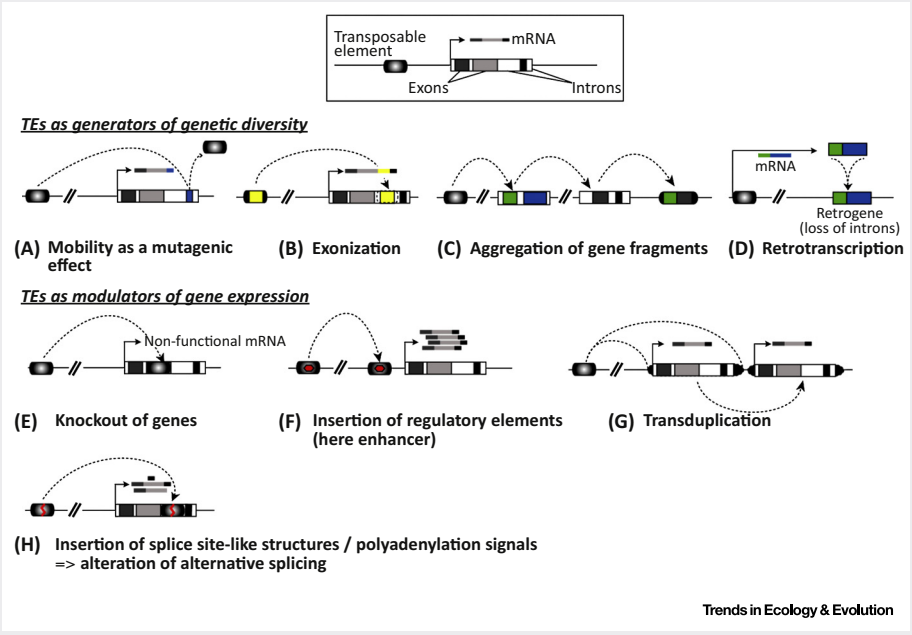


Figure I. Transposable Elements (TEs) as Generators of Genetic Diversity and Modulators of Gene Expression.

Phenotypic Consequences of TE and Epigenetic Activities

There are numerous pathways through which TEs can impact phenotypes, basically creating new proteins or affecting existing proteins' synthesis (Box 2). The most convincing evidence for TEs promoting adaptive phenotypic changes in response to global change arises from the vast literature on pests' rapid adaptation to agricultural chemicals [31]. For instance, in *Drosophila melanogaster* the *Accord* retrotransposon carrying a regulatory sequence has inserted upstream the insecticide resistance-conferring gene *Cyp6g1* resulting in the upregulation of

Cyp6g1 in tissues implied in detoxification [32]. Interestingly, when activated by the environment, TEs can also modify gene expression in response to stress to which the elements are themselves responsive [33,34]. For instance, in some plants (e.g., maize, rice) temperature-, salinity-, or UV-sensitive TEs were showed to be inserted in the flanking regions of some genes, inducing specific stress-responsive regulation of these genes [33,34].

In essence, epigenetics can promote 'on-demand' phenotypic variation by modulating the expression of the information encoded in the DNA sequence of somatic cells during development [6]. For instance, rapid physiological acclimation in the Antarctic polychaete *Spiophanes tcherniai* in response to warm stress is associated with modifications in global DNA methylation patterns [35]. Another example concerns the induction of drug resistance (i.e., hycanthone) in clones of the parasite *Schistosoma mansoni* previously exposed to sublethal doses [36]. The induced resistance was associated with several histone modifications over the genome and, more particularly, in the gene *SmMRP1* encoding a multidrug-resistance-associated protein [36]. These examples illustrate how epigenetics can promote acclimation to global change stressors. Patterns of DNA methylation can also persist across generations and produce heritable phenotypic changes [37–40]. For instance, Cortijo *et al.* [38] demonstrated that specific heritable methylation patterns in *Arabidopsis thaliana* experimental strains accounted for 60–90% of the heritability for flowering time and primary root length. In animals most (but not all) covalent modifications at nucleotides and histone tails are reset in primordial germ cells and in the zygote after fertilization (i.e., epigenetic reprogramming), hence limiting – but not completely preventing – the transmission of epigenetic marks to subsequent generations [39–41]. For instance, Anway *et al.* [39] demonstrated that environmental toxins induce heritable altered DNA methylation patterns associated with male infertility in exposed adult rats that are transmitted over at least four subsequent generations unexposed to the stress.

In summary, there is ample factual evidence that the activities of TEs and ECs are sensitive to stress, potentially accelerating adaptive (heritable or not) responses of organisms. These stressors include major components of global change such as climate, toxicants, and pests, which *de facto* suggests a non-negligible role of these mechanisms in organisms' responses to global change. We now review evidence for the tight links between TEs and ECs [11,13], which we believe is important to better appreciate the full potential of TEs and ECs in organisms' responses to global change.

Intimate Links between TEs and ECs

Reciprocal Control between TEs and Epigenetic Regulation

ECs are key in repressing TE activity, thus protecting genome integrity against TEs' disruptive mobility [13]. Many TEs are targeted by DNA methyltransferases and the arousal of epigenetic silencing is often associated with the activation of TEs [42,43], thus partly explaining the sensitivity of TEs to the environment [16].

Conversely, TEs contribute to the evolution of genetic and epigenetic regulatory networks [9,11,44]. Particularly, TEs escaping epigenetic silencing might proliferate and contribute to the spread of DNA fragments that can themselves be targeted by subsequent epigenetic regulation [9,45]. In mice, the insertion of an intracisternal A particle retrotransposon (IAP) upstream of the *Agouti* gene causes a shift from a wild-type agouti phenotype to a yellow coat phenotype. Yet, when the inserted IAP is silenced through hypermethylation, the agouti phenotype is partly recovered [46]. Interestingly, the methylated status of the IAP element is sensitive to bisphenol A, a widely used chemical in the plastic industries [47]. Neonatal exposure to bisphenol A decreases the methylation of the IAP element, hence switching on its transcriptional activity, resulting in mice expressing the yellow phenotype [47].

Noncoding RNAs (ncRNAs) Are Key Elements of epigenetic–TE Networks

ncRNAs are integral parts of the epigenetic regulatory machinery by interacting with enzymes involved in DNA methylation and histone tail modifications (Box 2). Interestingly, several ncRNAs are encoded by TEs or by endogenous genes that are likely to be derived from TEs [48,49]. Thus, TEs are key genomic components encoding elements involved in the epigenetic machinery [49]. Another aspect of ncRNAs encoded by TEs is that they can act to repress the proliferation of the TEs from which they originate following a sequence complementary match (i.e., TE silencing) [50]. Thus, epigenetically induced controls on the activities of ncRNAs constitute a pathway to modulate TE activities [49].

These exciting discoveries highlight that TEs and ECs intimately interact through numerous pathways and suggest their joint implication in organisms' responses to stress. In the next section, we propose a general molecular engine combining TEs with epigenetics (Figure 1, Key Figure) that might allow rapid phenotypic changes through a continuum from rapid and reversible responses (i.e., phenotypic plasticity) to long-lasting and irreversible responses (i.e., microevolution) to global change.

General TE–Epigenetic Engineering in Response to Global Change

Phenotypic Plasticity (Figure 1A)

ECs are major determinants of non-heritable phenotypic variation [6] by modulating gene expression during development in response to environmental changes in two main ways. First, ECs can blindly increase the range of phenotypes relative to environmental changes at the population level, hence randomly generating variants on which selection can act [51] (Figure 2A). Second, phenotypes can adjust to (and better fit) the novel environment if epigenetics reveal hidden phenotypes that are genetically encoded and historically present in the population (Figure 2B), hence constituting 'environmentally directed' responses of organisms to environmental changes [51]. ECs probably play a major role in storing genetic information for particular phenotypes in a silent state as long as epigenetic marks are faithfully transmitted across generations, hence generating so-called hidden genetic variation [52]. Environmentally induced epigenetic changes can reveal hidden genetic variation, which provides a mechanism for rapid adaptation [53].

Moreover, under stress TEs can be activated in somatic cells (either directly or through the arousal of their epigenetic control) thus producing non-heritable phenotypic variation among somatic cells within an organism [54]. This mechanism, called genetic mosaicism, can instantaneously generate adaptive phenotypic variation in response to stress, especially in long-lived organisms [54]. It is noteworthy, however, that in organisms capable of vegetative reproduction or budding (e.g., some plants, most corals), environmentally induced genetic mosaicism associated with TEs can also promote the emergence of new phenotypic lineages [55].

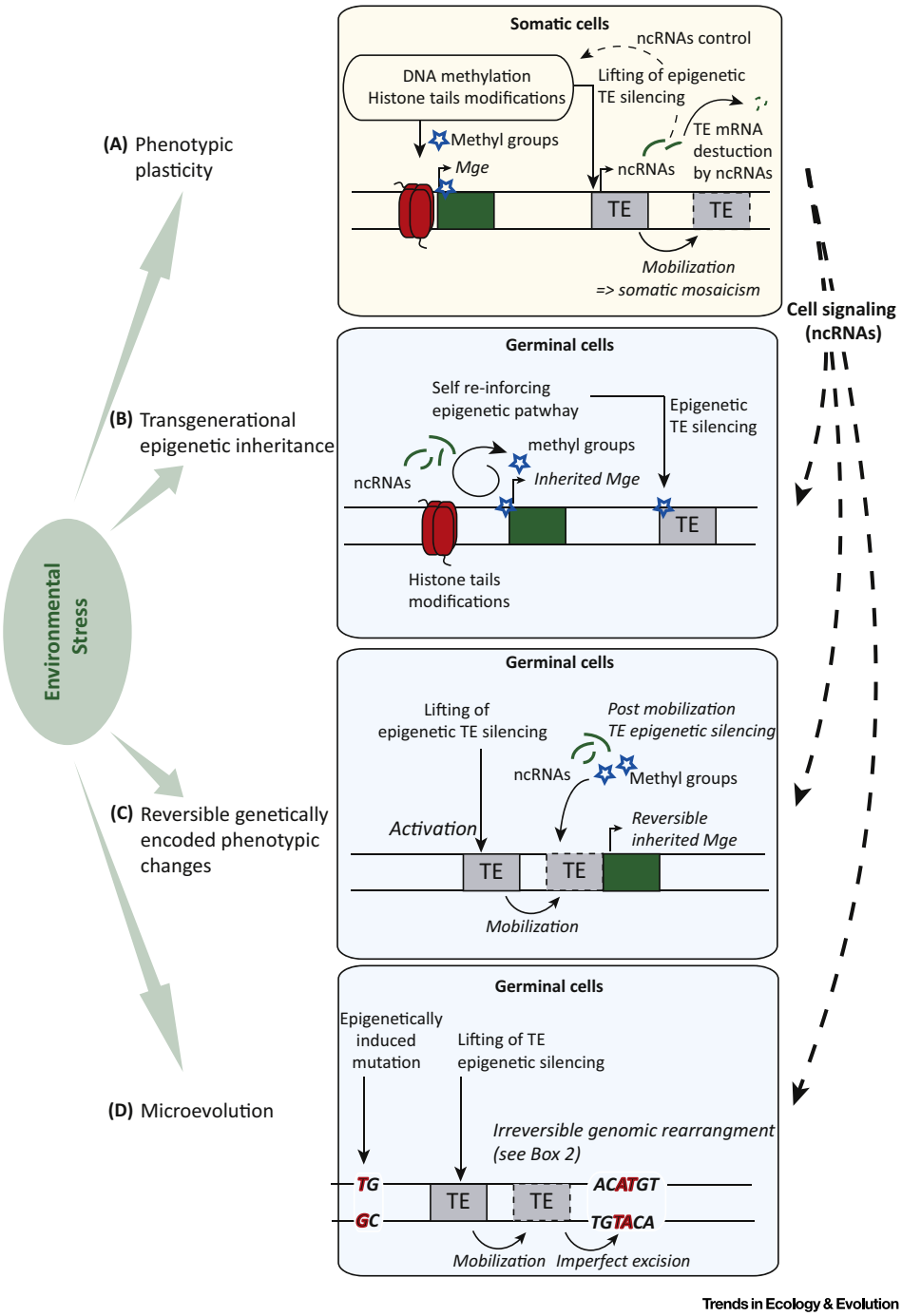
Transgenerational Epigenetic Inheritance (Figure 1B)

Accruing evidence indicates that epigenetics can be involved directly or indirectly in (micro) evolution when impacting germline cells: (i) variations in epigenetic patterns are ubiquitous; (ii) they can be associated with variations in fitness-related traits; and (iii) some are transmitted across generations, notably through a self-reinforcing pathway (Box 1) [4,56]. Moreover, epimutations generally occur at higher rates than mutations [57], and particularly so under stress [6,58], so that global change should promote rapid and heritable epigenetically induced phenotypic diversity [57,58].

Interestingly, when the environment stabilizes, epigenetic patterns might be stabilized and the associated phenotypes maintained in the population, thus giving time for natural selection to act on the genetic heritable component of phenotypic variation as soon as emerging genotypes get

Key Figure

The Transposable Element (TE)–Epigenetic Component (EC) Engine



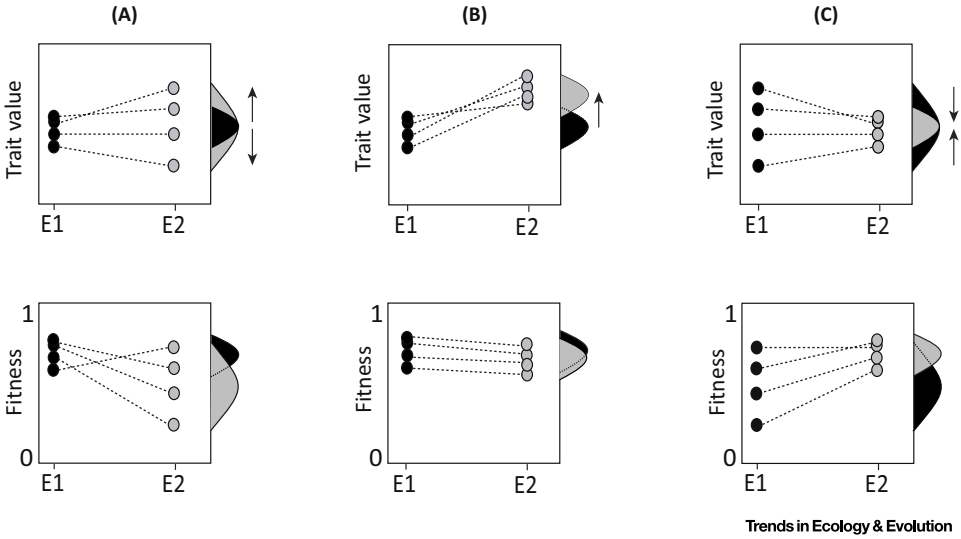


Figure 2. Evolutionary Outcomes of Epigenetically Induced Phenotypic Plasticity Under Stress. Upper panels: Individual reaction norms for a given phenotypic trait when the environment changes from E1 to E2. Black and grey dots are individual phenotypic trait values in E1 and E2, respectively. The population distributions of phenotypes in E1 and E2 are represented by the black and grey distributions respectively on the right of each panel. Arrows represent changes in the distribution of phenotypes at the population level after environmental changes. Lower panels: The evolutionary outcomes of the resulting phenotypic changes in terms of fitness at the individual (dots) and population (distributions on the right of each panel) level. (A) Epigenetic changes increase trait variance resulting in an increased fitness variance at the population level. Individuals with the optimal reaction norm are selected by natural selection. (B) Epigenetic changes affect the mean (but not the variance) of the trait towards a new optimum. (C) Epigenetic changes decrease trait variance around a new optimal value, which may lead to phenotypic canalization.

closer to a new optimal adaptive peak [59,60] (Figure 2C). Stabilizing epigenetic patterns also contribute to the inhibition of TE activity across generations, hence limiting the production of TE-induced genetic variation. This process might constitute a first step towards **phenotypic canalization** [59] and eventually genetic assimilation, the process by which a phenotype initially produced by means of a plastic response in a given environment becomes subsequently fixed irrespective of environmental conditions [61].

Reversible Genetically Encoded Phenotypic Changes (Figure 1C)

Transmission fidelity is lower for epigenetic marks than for genetic information (i.e., DNA sequences) and thus epimutations can lead to reversible phenotypes, notably in fluctuating environments [57]. Moreover, environmentally induced epigenetic changes might also generate

Figure 1. Evolutionary Outcomes of Activation of the TE–EC Engine in Somatic and Germinal Cells in Response to Stress. Mge, modified gene expression. (A) Under stress, activation of the TE–EC engine in somatic cells induces plastic responses through: (i) DNA methylation and/or modifications of histone tails; (ii) transcription of TE-encoded regulatory noncoding RNAs (ncRNAs); and (iii) lifting of epigenetic silencing and mobilization of TEs in somatic cells, leading to somatic mosaicism. (B) Stress induces epigenetic modifications in germline cells. The resulting phenotypes can be stabilized over generations (transgenerational epigenetic inheritance) through self-reinforcing epigenetic pathways (Box 1). Stress perceived in somatic cells can also induce the production of circulating ncRNAs that may modify the epigenome of remote germline cells [dashed arrow from (A) to (B)]. (C) Stress can induce the lifting of epigenetic silencing of TEs in germinal cells, resulting in the mobilization of TEs across the genome. The resulting phenotypes are thus transmitted to the next generations. However, because newly inserted TEs are targets for epigenetic silencing, the resulting heritable phenotypes are expected to be, in some cases, reversible. Similarly to (B), stress perceived in somatic cells can induce the production of circulating ncRNAs that may modify the epigenome of remote germline cells [dashed arrow from (A) to (C)]. (D) Stress can induce modifications of epigenetic patterns that can result in irreversible genomic changes either directly (mutagenic effect of epigenetic patterns) or indirectly through the release of epigenetic silencing of TEs and the resulting mobilization of TEs throughout the genome. As in (B) and (C), stress perceived in somatic cells can induce the production of circulating ncRNAs that may modify the epigenome of remote germline cells [dashed arrow from (A) to (D)].

transgenerational phenotypic changes by activating TEs, which in turn generates genomic modifications. New phenotypic variants originating from TE mobilization in the germline are stably embedded within the DNA sequence and can therefore be efficiently selected for. Yet, newly inserted TEs constitute specific targets for epigenetic regulation [9], so that emerging phenotypes resulting from TE mobilization might be at least partly reversible through post-insertional TE epigenetic regulation [47]. As a result, the interplay between EC and TE activity not only generates new phenotypes but also provides new regulatory pathways to modulate the expression of emerging phenotypes [9] and thus appears to be a major driver for the evolution of epigenetically controlled reaction norms.

Stable Genetically Encoded Phenotypic Changes: Microevolution (Figure 1D)

Finally, environmentally induced changes in TE activity and ECs can also generate irreversible genetic modifications (Boxes 1 and 2). When occurring in the germline, the resulting variants are subject to natural selection. It is thus expected that the production of genetic variability might be particularly boosted in response to global change [13,58].

From Phenotypic Plasticity to Inherited Phenotypic Changes

The sensitivity of the TE–epigenetic engine to environmental stressors provides a way for the genome to transmit information about environmental conditions across generations, meaning that phenotypic changes might not only rely on genetic variants emerging stochastically but may also be partly triggered by the environment [58]. Although still controversial, there is increasing empirical support for this idea [6,40,62]. Certainly the best illustration concerns the recent experimental demonstration that specific odor fear conditioning in mice is transmitted to subsequent generations, even when removed from parental environmental perturbation, without changes in DNA sequence [40]. The parental odor fear conditioning induces a heritable hypomethylation at the *Olf151* gene encoding the M71 odorant receptor in the paternal gametes, which generates over-transcription of *Olf151* in the resulting hypersensitive F1 and F2 offspring [40].

How environmental conditions mainly perceived by somatic cells can promote heritable and adaptive phenotypic variation remains an intriguing question. Recent studies partially tackled this question by revealing the existence of circulating ncRNAs expressed in neurons and triggering changes in epigenetic patterns in the distant germline that remain present 25 generations later [62]. In plants, siRNAs expressed in shoot cells (i.e., from photosynthetic organs) can move to root cells (i.e., water-providing organs) and modify DNA methylation profiles in the latter cells, hence providing a coordinating system between functional organs [63]. Similarly, expressed miRNAs in stressed somatic cells can move to germ cells and locally modulate epigenetics, and eventually activate TEs [64] (dashed arrows in Figure 1). This soma-to-germline cell communication pathway constitutes an amazing process to fine-tune the production of heritable genetic/phenotypic variation fitting the environment perceived by organisms.

Concluding Remarks

TEs and ECs can be integrated into a single broad environment-sensitive molecular engine potentially allowing organisms to respond to global change, notably by: (i) fine-tuning the phenotype in a real-time fashion; (ii) adjusting the production of heritable phenotypic and genetic variation; and (iii) producing heritable phenotypes with different levels of transmission fidelity depending on the acting selecting pressure [13,58]. TEs and ECs have already been proposed as key players in fostering phenotypic and biological innovations during major ecological transitions [11–14]. Global change is considered such an ongoing major ecological transition [17] that – we believe – might trigger the TE–epigenetic engine and thus boost organisms' evolutionary responses to contemporary environmental changes.

Outstanding Questions

To what extent do genetic and phenotypic variations produced by the TE–EC engine contribute to variation in fitness-related traits?

What is the 'effect size' of the TE–EC engine relative to other mechanisms (selection on standing genetic variation, genomic rearrangements and mutations) involved in responses to global change?

How much does this effect size vary among organisms? Which organisms are more prone to be under the influence of this engine?

Are there global change stressors (e.g., pollution, climate change, fragmentation, invasion) that may preferentially activate the TE–epigenetic engine?

How do demographic parameters (effective population size) influence the effects of the TE–EC engine in organisms' response to global change at the population level?

The reality of this TE–EC engine is supported by accruing scientific evidence that TEs and ECs are sensitive to several global change stressors and are triggering genomic and phenotypic responses to these stressors. Although the individual effects of TEs and ECs on rapid phenotypic adaptation are increasingly acknowledged [4,65], much is to be done to demonstrate causal links between the TE–EC engine and organisms' responses to global change (see Outstanding Questions). To date, rapid and on-demand adaptation to global change has been largely proved in the bacteria world. In particular, integrons associated with TEs are key players in the emergence of antibiotic-multiresistant bacteria, which constitute a major public health concern [66]. Future research on eukaryotes should be inspired by the recent progresses in prokaryotes regarding the importance of the TE–epigenetic engine as a driver or rapid adaptation to global change.

Several avenues can make this exploration a functional tool for evolutionary ecologists. First, the increasing availability of biotechnologies and databases revealing the genomic distribution of

Box 3. Considering Examples of Valuable Biological Models to Test the Relevance of the TE–EC Engine in Promoting Rapid Response to Global Change

To investigate the role of the TE–epigenetic engine in responses to global change we believe organisms should display four characteristics; they must: (i) be sensitive to global change stressors (e.g., chemicals, global warming); (ii) respond phenotypically to these stressors; (iii) be easy to manipulate under experimental conditions; and (iv) dispose of genomic resources to facilitate the monitoring of genomic changes. We propose a series of three organisms (see below) sharing these characteristics that could pioneer empirical research on the links between the TE–epigenetic engine and responses to global change.

Corals are highly sensitive to global warming and ocean acidification [81]. Somatic mutations could be an important evolutionary pathway for budding colonial reef corals to adapt rapidly to the current oceanic challenges [82]. By fostering genomic changes in somatic cells, it is likely that TEs previously found to be activated through heat stress in the coral *Montastraea faveolata* (Figure IA) [83] could play a crucial role in reef coral adaptation to changes in marine conditions.

Rapid adaptation of birds to global change is widely documented [84,85]. TEs are relatively scarce in birds compared with other vertebrates and are likely to hardly affect bird genomes [86]. However, Liebl *et al.* [84] demonstrated that invasive populations of *Passer domesticus* (Figure IB) display high epigenetic diversity possibly associated with phenotypic variation. Similarly, it is very likely that epimutations play a role in the observed rapid phenotypic response of bird populations to climatic change, such as changes in phenology in the great tits in response to warming temperatures [85].

Invasive populations can benefit from the admixture resulting from multiple introductions of genetically distinct native populations increasing their adaptive potential [87]. For instance, multiple introductions of *Phalaris arundinacea* (Figure IC) in North America has promoted the emergence of highly diversified genotypes compared with the native, with higher vegetation colonization ability and phenotypic plasticity [87]. Nonexclusively, the TE–epigenetic network might have also contributed to the rapid evolution of *P. arundinacea* invasive populations. Environmental challenges and genomic shocks (e.g., hybridization) promote bursts of TE mobilization and newly inserted TEs are prime targets for epigenetics, promoting the evolution of phenotypic plasticity. Thus, invasive genotypes of *P. arundinacea* could have benefited from the environmentally induced mobilization of TEs into or near genes associated with key phenotypic traits. Moreover, the post-insertional epigenetic regulation of TEs might have promoted the observed evolution of trait plasticity.

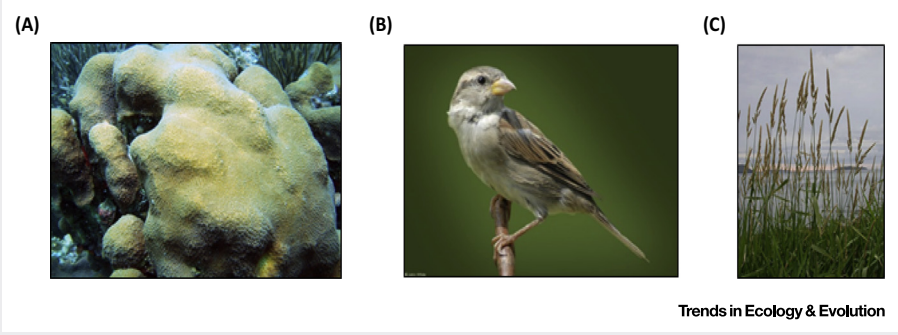


Figure I.

TEs and ECs in a wide range of organisms [67,68] should help in determining the extent to which these elements are distributed among the tree of life and how they jointly interact with the genomes. Second, a powerful approach to establish causalities implies the use of experimental evolution jointly monitoring modifications at the phenotypic and genomic levels (with a focus on the TE–epigenetic machinery) in organisms challenged with global change stressors. Asexual organisms would be particularly relevant because the possible effects of gene rearrangements on emerging phenotypes are drastically reduced. Third, several molecular engineering tools could help demonstrate the causality between the TE–epigenetic engine and organisms' responses to global change. For instance, the causal implication of epigenetics in inbreeding depression was established in the plant *Scabiosa columbaria* where a demethylating agent (i.e., 5-azacytidine) restored depressed traits in inbred seeds [69] (see also [70] for a review on molecular engineering involving TEs).

These analytical and experimental approaches should primarily be applied to species that have been shown to reply adaptively to global change and for which the role of the TE–epigenetic engine can be suspected (Box 3). Since not all species are similar with regard to the composition of their genomes in TEs and epigenetics [15], we predict that this molecular toolbox should greatly help in highlighting the unsuspected diversity of molecular mechanisms of adaptation, thus demonstrating the reality of our proposed TE–epigenetic engine of rapid adaptation to global change.

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