15 Evolutionary Change Is Naturally Biological and Purposeful

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Overview

In trying to remove any innate biological action so that natural selection could be the only determinant directing evolutionary change, Darwin's followers in the twentieth century obliged themselves to assume that gradual selected accumulation of character changes due to random mutations could produce major differences in morphology, metabolism, and behavior over long periods of time. This process, phyletic gradualism, was proposed to account for all evolutionary diversity without any biological agency. However, the gradualist view of evolutionary change could not accommodate cytogenetic and genomic evidence that living organisms possess internal capacities for making large-scale modifications to their heredity and phenotype. In. particular, McClintock's discovery in the late 1940s of transposable controlling elements that could move to new genomic positions and alter the expression of nearby coding sequences solved an evolutionary problem that was virtually impossible to explain by phyletic gradualism: the formation of coordinately regulated multilocus systems connected by shared transcription factor binding sites. Molecular genomic data in this century has confirmed the roles of transposable elements in formatting expression of new genomic networks at key stages in evolutionary change. Moreover, the movement of the various types of transposable elements to new genome locations is triggered by ecological challenge and organismal stress. Thus, mobile DNA cassettes serve as dedicated change operators when evolutionary transformation functions capable of causing major genome rewriting under stress are essential purposive tools needed for life to survive in dynamic ecologies.

15.1 Introduction

As students, we are taught that the idea of goal-directed activities—teleology or teleonomy (Pittendrigh, 1958)—is unscientific. We learn that the natural world has no inherent drives or purposeful actions, and we are further taught that to believe such nonmaterial impulses exist is to indulge in anthropomorphizing nature. Nowhere was the word *teleology* such a forbidden term as among mainstream neo-Darwinian evolutionary biologists. Their attempts to deny biological purposefulness or agency in any form were complete mysteries to me. I could see

plenty of functionality and intentionality in all fields of the life sciences,[1] and informatics/cybernetics has taught us that not all natural phenomena are material (Corning, 2007; Wiener, 1965). It seemed to me that many neo-Darwinists turned themselves into intellectual and linguistic contortionists when they discussed biological action. The following quotation from a 2014 blog post by my well-known emeritus colleague at the University of Chicago, Jerry Coyne, is an illustration of what I mean.

> Among virtually all scientists, dualism is dead. Our thoughts and actions are the outputs of a computer made of meat—our brain—a computer that must obey the laws of physics. Our choices, therefore, must also obey those laws. This puts paid to the traditional idea of dualistic or "libertarian" free will: that our lives comprise a series of decisions in which **we could have chosen otherwise**. We know now that we can never do otherwise, and we know it in two ways.
>
> The first is from scientific experience, which shows no evidence for a mind separate from the physical brain. This means that "I"—whatever "I" means—may have the *illusion* of choosing, but my choices are in principle predictable by the laws of physics, excepting any quantum indeterminacy that acts in my neurons. In short, the traditional notion of free will—defined by Anthony Cashmore as "a belief that there is a component to biological behavior that is something more than the unavoidable consequences of the genetic and environmental history of the individual and the possible stochastic laws of nature"—is dead on arrival.
>
> The illusion of agency is so powerful that even strong incompatibilists like myself will always act as if we had choices, even though we know that we don't. We have no choice in this matter. But we can at least ponder why evolution might have bequeathed us such a powerful illusion.
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> —Coyne, J. A. (2014). On free will, in answer to the question, What scientific idea is ready for retirement? (https://www.edge.org/response-detail/25381)

15.2 The Delusion of Physical Bottoms-Up Reductionism: A Commitment to Natural Selection as the Unique Guiding Force in Evolution

Coyne's denial of human agency or choice, naming both as illusory artifacts of "libertarian" dualism, is a stunning example of physical reductionism run amok. What kind of thinking lies behind such an extreme declaration? I only realized the answer to that question when I was asked to write an extended definition of "evolution" for the SAGE *Encyclopedia of Theory in Science, Technology, Engineering, and Mathematics*. The exercise obliged me to examine the basic tenets of the neo-Darwinian modern synthesis and explain why it failed to incorporate much of what we have learned from genome sequence data and other aspects of molecular biology and genetics (Shapiro & Noble, 2021). The appeal to natural selection as a guiding principle was meant to replace Larmarck's internal and immaterial "le pouvoir de la vie" that was supposed to drive evolution toward more complex life forms (Lamarck, 1994). Among twentieth-century neo-Darwinists, natural selection and random mutation were also invoked to replace Lamarck's "L'influence des circonstances," which guided hereditary variation by use and disuse of particular traits, an idea that Darwin had fully accepted in *The Origin of Species* (Darwin, 1859). I came to see that the determination of Darwin's twentieth-century followers to eliminate any internal (i.e., biological) drives and make natural selection the sole determinant of direction in evolutionary change imposed stringent limits on their ability to explain the origins of biological processes.

Assigning to natural selection the sole responsibility for determining the course of hereditary variation meant that mutations had to be random events, devoid of organic causation,

and of small effect on the character of the organism. This was the founding principle of phyletic gradualism. As Darwin wrote in chapter 6 of the first edition of *The Origin of Species*, "if it could be demonstrated that any complex organ existed, which could not possibly have been formed by numerous, successive, slight modifications, my theory would absolutely break down. But I can find out no such case" (Darwin, 1859). It was this overly simplified view of evolutionary change adopted for theoretical reasons and devoid of any biological input[2] that forced the neo-Darwinists like Coyne to invoke a purely physicalist model of how organisms evolve. There was consequently no place in the conceptual framework of the modern synthesis for biologically mediated punctuated (saltatory) evolutionary change, as proposed by non-Darwinian evolutionists like Hugo de Vries or Richard Goldschmidt (de Vries, 1905; Goldschmidt, 1940), or for responses by evolving organisms to inputs from ecological fluctuations. In addition, the modern synthesis was based on the mid-twentieth-century idea that "genes are the basic units of all living things" (Beadle, 1948). Accordingly, an organism's genome was conceptualized as a collection of more or less independent gene units subject to their individual random gene mutations.

15.3 How Did Discoveries After the Modern Synthesis Reveal the Neo-Darwinian Emphasis on Natural Selection to Be a Problem in Practical and Theoretical Evolution Science?

The fundamental epistemological error of the neo-Darwinists was to believe that they could abstract evolution away from any causative biological component. The idea that forbidding biological goals, agency, and intentionality to make their theoretical constructs more rigorous was to confuse purely mechanical accounts with scientific explanations. In their desire to eliminate "libertarian dualism," evolutionists such as Coyne have had to ignore mounting empirical evidence demonstrating the activity of numerous cellular and biomolecular processes capable of changing the structure and content of genomes (Shapiro, 2013; Shapiro, 2017; Shapiro, 2019; Shapiro & Noble, 2021; Shapiro, 2022).

To select one of the most important genome-change processes for detailed discussion, we will focus on the work of Barbara McClintock and genomic validation of her ideas. In the late 1940s, McClintock unexpectedly discovered that extreme genome stress could induce her maize plants to activate normally dormant "controlling elements," which can transpose from one position in the genome to other positions and alter the regulation and expression of adjacent genetic loci (McClintock, 1950; McClintock, 1952; McClintock, 1987). Transpositions and chromosome rearrangements associated with these elements were a far cry from the random gene mutations envisaged by the modern synthesis. Consequently, in the 1950s and 1960s, McClintock's work received a hostile and incredulous reception. Nonetheless, molecular and genomic studies beginning in the 1960s confirmed the presence of comparable transposable DNA elements playing important roles in evolution in all types of living organisms, from the simplest bacteria and archaea to higher plants and animals, and she received the Nobel Prize for her discovery in 1983 (Bukhari et al., 1977; McClintock, 1984; Shapiro, 1983). Mobile DNA elements (sometimes called "jumping genes") analogous to McClintock's come in a variety of forms: (1) DNA transposons that move as DNA and have defined ends, (2) retroviruses and structurally related retrotransposons with long terminal repeats (LTRs)

integrated into the genome which move via RNA intermediates with defined ends, and (3) non-LTR retrotransposons which move via RNA intermediates that do not require defined ends (Bourque et al., 2018). To buttress his 1859 view of phyletic gradualism, Darwin had quoted Linnaeus' dictum *Natura non facit saltus* ("Nature does not make jumps") in *The Origin of Species* (Darwin, 1859). However, the prestige and authority of Linnaeus and Darwin notwithstanding, McClintock and her followers demonstrated that when it comes to genomic DNA, nature does indeed literally make jumps, and life has evolved several different molecular mechanisms to make those jumps take place.

Their dedication to natural selection led neo-Darwinists like Coyne to deny well-documented sensory, cognitive, computational, and decision-making abilities in living organisms. In doing so, they discounted the discoveries about intricately organized biological soft matter that molecular genetics revealed to exist and to exercise sensory, regulatory, and computational processes in even the simplest living organisms (Bray, 2009; Regolin & Vallortigara, 2021). These biological systems often display a sensitivity and robustness that far exceed the products of modern technology (Bray, 2012; Bray, 2015). In the interval between the mid-twentieth century and the third decade of the twenty-first century, we have experienced a theoretical revolution in our understanding of inherited organismal traits. In particular, we have abandoned one-gene, one-trait notions based on individual genes as "the basic units of life" (Beadle, 1948), instead embracing what has come to be called *complex systems biology* (Bornholdt, 2001; Pattee, 1973; Toussaint & von Seelen, 2007). Biological traits are currently viewed from the perspective of the genomic networks that encode and regulate the formation and operation of multicomponent functional systems and structures in all organisms (Bray, 2003; Heng, 2008; Maslowska, Makiela-Dzbenska, & Fijalkowska, 2019; Pal et al., 2017; Pezzulo & Levin, 2016). This network perspective is particularly relevant, for example, to thinking about the evolution of multicellular development (evo-devo) (Bowman, Briginshaw, & Florent, 2019; Rebeiz, Patel, & Hinman, 2015).

15.3.1 Genetic Regulatory Studies Indicate How Mobile DNA Elements Contribute to Hereditary Network Evolution

McClintock's genetic studies were far from the only research revolutionizing our understanding of genetics. At the same time as McClintock was working out the details of controlling-element action, Jacques Monod and his colleagues at the Institut Pasteur in Paris began studying the regulation of protein synthesis in bacteria (Jacob & Monod, 1961). They and their successors discovered novel noncoding genetic elements that were central to the control of transcription and genome expression (Reznikoff, 1992). These noncoding elements included DNA sequences recognized by DNA-binding proteins now generically known as transcription factors (TFs), which control and coordinate messenger mRNA synthesis from selected coding sequences as organisms elaborate complex traits and structures (Bondos & Tan, 2001; Sprague, 1991; Zhang et al., 2005). A key feature of the underlying genomic expression networks is the presence of shared TF binding-site DNA sequences controlling transcription at coding regions located at multiple places within the genome. These TF binding sites are now designated as *cis*-regulatory modules or CRMs (Pauls et al., 2015; Schwarzer & Spitz, 2014; Suryamohan & Halfon, 2015). It is very difficult to imagine how random mutations and phyletic gradualism could generate the functionally significant numbers of shared CRMs that appear at unlinked genetic loci encoding different proteins. The collective probability of the

same sequence motifs independently evolving *ab initio* at multiple genomic locations is the product of their individual probabilities, and this product rapidly becomes impossibly small as the number of shared distal CRMs increases. However, the ability of controlling elements to transpose to multiple genome sites provides a feasible solution to the problem of organizing or wiring transcriptional networks across genomes (Rebollo, Romanish, & Mager, 2012).

In the twenty-first century, evolution research is chiefly based upon genome sequencing. As empirical scientists, we are obliged to ask: What does the genomic evidence have to say about saltatory network evolution by mobile DNA action? The answer is quite a bit, in fact, and the number and documentation of the roles that mobile DNA plays in plant and animal evolution increase every year. The presence of TF binding sequences in mobile DNA elements had been noted early in the twenty-first century (Bolotin et al., 2011; Bourque et al., 2008; Jordan et al., 2003; Polak & Domany, 2006; Polavarapu et al., 2008; van de Lagemaat et al., 2003). Genome researchers also noted early on that control sites derived from mobile elements are phylogenetically distinct. For example, one early study noted that "human-mouse genome wide sequence comparisons reveal that the regulatory sequences that are contributed by TEs are exceptionally lineage specific" (Marino-Ramirez et al., 2005). A decade after the publication of the initial draft of the human genome sequence (Lander et al., 2001), comparison of 29 mammalian genomes identified more than 280,000 examples of CRMs derived from all classes of transposable DNA elements in our genome (Lindblad-Toh et al., 2011; Lowe et al., 2011). A 2014 paper analyzing CRMs in the mouse and human genomes confirmed the species-specificity of transposable DNA-derived elements and found that anywhere from 2% to 40% of all genomic binding sites could be traced to mobile DNA insertions, depending on the particular TF bound (Sundaram et al., 2014).

Table 15.1 summarizes the range and diversity of biological characteristics that have been attributed to mobile DNA-derived networks. The cases are notable for the range of organisms (a single-celled diatom to complex multicellular plants and vertebrates) and the biological importance of the systems affected, including gamete formation (germline development, flowering), early embryonic development (gastrulation, stem cell pluripotency), embryo development and nourishment (placenta, endosperm), body plan development, and nervous system formation. The phylogenetic distribution of a particular family of mobile elements indicates when it appeared in evolutionary history (Jurka et al., 2012). For example, "at least 16% of eutherian specific CNEs (conserved non-coding elements) overlap currently recognized transposable elements in human" (Mikkelsen et al., 2007). That kind of phylogenetic "dating" is how many of the examples in table 15.1 were assigned to the formation of a specific taxonomic group, such as animals, vertebrates, mammals, eutherian mammals, or primates (Jacques, Jeyakani, & Bourque, 2013). The connection between an ancient group of mobile DNA elements in multiple genomes and a certain kind of function, such as body plan development, forms the basis for the conclusion that those elements helped wire the control network at a particular evolutionary transition (Riegler, 2008). The evidence for positive selection operating on many recent mobile DNA element insertions indicates that the changes were truly of adaptive evolutionary benefit (Lowe, Bejerano, & Haussler, 2007; Rishishwar et al., 2018; Saber et al., 2016).

Mobile DNA elements contribute to genomic networks in other ways than just providing distributed TF binding sites. The protein coding sequences of mobile DNA elements have also been evolutionary precursors to a broad range of functionally different proteins

Table 15.1
Distributed genome network innovations attributed to mobile DNA elements

Organism	Transposable DNA-Modified System(s)	References
18 fungal genomes	Whole-genome architecture and transcriptional profiles	(Castanera et al., 2016)
Diatom *Phaeodactylum tricornutum*	Responses to nitrate starvation and exposure to diatom-derived reactive aldehyde-induced stress	(Maumus et al., 2009; Oliver, Schofield, & Bidle, 2010)
Leishmania	Post-transcriptional regulation	(Bringaud et al., 2007)
PLANTS		
Plants	Genome evolution	(Bennetzen & Wang, 2014; Qiu & Köhler, 2020)
Plants	Epigenetic controls	(Lisch & Bennetzen, 2011)
Plants	Stress responses	(Hou et al., 2019; Negi, Rai, & Suprasanna, 2016)
Peaches, almonds	Evolutionary genome differences	(Alioto et al., 2020)
Grasses	C4 photosynthesis	(Cao et al., 2016)
Maize	Abiotic stress response	(Lv et al., 2019; Makarevitch et al., 2015; Ramachandran et al. 2020)
Maize	Helitron transposons "reshuffle the transcriptome"	(Barbaglia et al., 2012)
Maize	25% of DNAse1-hypersensitive sites (actively transcribed loci) evolved from mobile DNA insertions	(Zhao et al., 2018)
Cotton	Fiber cell development	(Wang et al., 2016)
Tomato	Ripening	(Jouffroy et al., 2016)
Coffea	Drought stress response	(Lopes et al., 2013)
Arabidopsis	Abiotic stress (phosphate limitation, high salt, freezing temperatures, arsenic toxicity)	(Joly-Lopez et al., 2016; Joly-Lopez et al., 2017)
Arabidopsis	Flower development	(Baud et al., 2020; Muino et al., 2016)
Arabidopsis	Endosperm development (functionally comparable to mammalian placenta)	(Batista et al., 2019; Qiu and Köhler, 2020)
Pine	"Transposable element interconnected gene networks"	(Voronova et al., 2020)
ANIMALS		
Metazoa	Evolutionary innovation	(Nishihara, 2020; Piskurek & Jackson, 2012)
Drosophila	Malathion insecticide resistance	(Salces-Ortiz et al., 2020)

Drosophila	X chromosome dosage compensation	(Ellison & Bachtrog, 2019; Ellison & Bachtrog, 2013)
Drosophila	Early embryonic development	(Spirov, Zagriychuk, & Holloway, 2014)
Vertebrates	Evolutionary innovation	(Etchegaray et al., 2021; Warren et al., 2015)
Vertebrates	Body plan development	(McEwen et al., 2009; Woolfe & Elgar, 2008)
Zebrafish	p53 response network	(Micale et al., 2012)
Fish	Migratory behavior	(Carotti et al., 2021)
Mammals	TET-controlled passive DNA demethylation	(Mulholland et al., 2020)
Mammals	Estrogen receptor network	(Testori et al., 2012)
Mammals	Uterine development, pregnancy	(Lynch et al., 2011; Lynch et al., 2015)
Mammals	Placental development (species-specific elements in mouse and humans)	(Chuong, 2013; Chuong & Feschotte, 2013; Chuong et al., 2013; Chuong, 2018; Dunn-Fletcher et al., 2018; Frank & Feschotte, 2017; Sakurai et al., 2017; Sun et al., 2021; Zhang & Muglia, 2021)
Mammals	Convergent evolution of prolactin expression with different mobile DNA insertions	(Emera et al., 2012)
Mammals	Mammary gland development	(Nishihara, 2019)
Mammals	X-inactivation in females	(Elisaphenko et al., 2008; Kannan et al., 2015; Lyon, 2000; Lyon, 2003)
Mammals	Innate immunity	(Chen et al., 2019; Chuong, Elde, & Feschotte, 2016; Srinivasachar Badarinarayan & Sauter, 2021)
Mammals	Wnt5a expression in mammalian secondary palate controlled by complex enhancer evolved from "coordinately co-opted" transposable elements	(Nishihara et al., 2016)
Mammals	Basic mammalian morphology and body plan development	(Hirakawa et al., 2009; Okada et al., 2010)
Mammals	Brain and nervous system development	(Bejerano et al., 2006; Ferrari et al., 2021; Lapp & Hunter, 2016; McEwen et al., 2009; Nakanishi et al., 2012; Notwell et al., 2015; Policarpi et al., 2017; Santangelo et al., 2007; Sasaki et al., 2008; Tashiro et al., 2011)
Eutherian mammals	Eutherian-specific morphology and neural development	(Polychronopoulos et al., 2017)
Eutherian mammals	"at least 16% of eutherian-specific CNEs overlap currently recognized transposable elements in human"	(Mikkelsen et al., 2007)
Bat *Myotis velifer*	Cell migration, gastrulation (weaker signals for Wnt signaling, artery and heart valve morphogenesis, neural crest differentiation)	(Cosby et al., 2021)

(*continued*)

Table 15.1
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Organism	Transposable DNA-Modified System(s)	References
Mouse	RNA polymerase PolII- or PolIII-specific insulator-bounded subnuclear domains	(Roman, Gonzalez-Rico, & Fernandez-Salguero, 2011a; Roman et al., 2011b)
Mouse	Circadian rhythms	(Cosby et al., 2021)
Mouse	Mouse germline development and specificity	(Maezawa et al., 2020)
Mouse	Visual cortex development	(Lennartsson et al., 2015)
Primates	Primate-specific innovations arose chiefly by positively selected mobile DNA element insertions	(Jacques, Jeyakani, & Bourque, 2013; Rishishwar et al., 2018; Trizzino et al., 2017)
Anthropoids	Brain and eye development	(del Rosario, Rayan, & Prabhakar, 2014)
Human	Insulator-bound subnuclear domains	(Wang et al., 2015)
Human	c-Myc regulatory subnetwork	(Wang et al., 2009)
Human	P53 response network	(Cui, Sirotin, & Zhurkin, 2011)
Human	Germline development	(Liu & Eiden, 2011; Sakashita et al., 2020)
Human	Embryonic development	(Kunarso et al., 2010; Wang et al., 2014; Xiang & Liang, 2021)
Human	Stem cell pluripotency	(Izsvak et al., 2016; Lu et al., 2014; Römer et al., 2017; Santoni, Guerra, & Luban 2012; Sexton, Tillett, & Han, 2021; Torres-Padilla, 2020)
Human	Zygotic genome activation and preimplantation embryonic development	(Fu, Ma, & Liu, 2019; Fu et al., 2021; Grow et al., 2015)
Human	Cell type- and tissue-specific expression	(Huda et al., 2011a; Huda et al., 2011b; Jjingo et al., 2011)
Human	Tissue-specific expression of regulatory long non-coding lncRNAs	(Chishima, Iwakiri, & Hamada, 2018)

(Etchegaray et al., 2021; Naville et al., 2016; Volff, 2006). Of particular relevance to the elaboration of genomic networks are those cases involving mobile element proteins that bind to specific sequences at the ends of the DNA being inserted into a new target site. A number of these transposases and integrases have contributed to the evolution of regulatory proteins controlling transcription. One way this has happened is by forming a chimeric fusion protein of the transposase DNA-binding domain with the non-DNA-binding domains of an existing TF, such as the fusions in higher vertebrates to regulatory domains of abundant zinc finger proteins (Cosby et al., 2021; Ecco et al., 2016; Ecco, Imbeault, & Trono, 2017). Such a fusion automatically transforms the corresponding mobile DNA element termini throughout the genome into CRMs responding to the new chimeric TF. The most recent study on this topic reports the independent formation of such mobile DNA-host TF fusion proteins to have occurred at least 22 times in the coelacanth, 90 times in amphibians, 313 times in reptiles, 92 times in birds, 31 times in the platypus, 106 times in marsupials, and 928 times in eutherian mammals (Cosby et al., 2021).[3]

15.3.2 How the Formation and Function of Mobile Element-Based Networks Connect to a Changing Ecology in Evolution

Another outdated feature of the physicalist/reductionist neo-Darwinian account is the exclusion of any influence of life history events from any role in evolutionary change. Part of this position comes from making natural selection the sole outside influence on the course of evolution, and another part comes from a rejection of the Lamarckian notion (even though it was shared by Darwin!) that "use and disuse" has an influence on the acquisition, exaggeration, or disappearance of particular traits (Darwin, 1859; Lamarck, 1994). However, today we recognize that all organisms have sensory and signal transduction systems to monitor their internal processes and environmental interactions and adjust their physiologies, growth, reproduction, and self-repair functions accordingly (Bray, 2009; Regolin & Vallortigara, 2021; Shapiro, 2020). These sensory capabilities can also influence the transpositional activities of mobile DNA elements as well as the expression of any resulting genomic networks.

Table 15.2 lists some of the many conditions documented to stimulate mobile element spreading in a variety of organisms (see also Negi et al., 2016, and https://shapiro.bsd.uchicago.edu/Ecological_Factors_that_Induce_Mutagenic_DNA_Repair_or_Modulate_NGE_Responses.html for additional references). There are two major factors stimulating mobile DNA activity evident in the examples from table 15.2: (1) biotic and abiotic stresses and (2) interspecific hybridization, which often leads to polyploidization (Vicient & Casacuberta, 2017). The significance of such inputs is to increase genomic innovation by mobile DNA when the conditions of life are most difficult. Note that interspecific hybridization is an indicator of such difficulty because it is most likely to occur when the within-species mating pool has declined. A more basic point to remember in thinking about evolutionary theory is that artificial generation of novel species has been practiced in agriculture for thousands of years by interspecific hybridization, never by selection alone (Anderson, 1954; Stebbins, 1951). By these observations alone, we are obliged to say that the selection-based neo-Darwinian paradigm has not been empirically verified.

Stress-induced genome reformatting is just the kind of feedback response we would expect if mobile DNA had the function of providing adaptive variability and genomic diversity when most necessary. In addition, the recently transposed elements provide a molecular genomic

Table 15.2
Stimuli reported to trigger increased mobile DNA activities

Organism	Stimulus	Reference(s)
BACTERIA		
Bacterium *Deinococcus geothermalis*	Oxidative stress	(Lee, Choo, & Lee, 2020; Lee et al., 2021)
Bacterium *Geobacillus kaustophilus*	Heat stress	(Suzuki et al., 2021)
Bacterium *Cupriavidus metallidurans*	Zinc exposure	(Vandecraen et al., 2016)
FUNGI		
Yeast *Saccharomyces cerevisae*	Adenine starvation	(Servant, Pennetier, & Lesage, 2008; Todeschini et al., 2005)
Yeast *Saccharomyces cerevisae*	Ionizing radiation	(Sacerdot et al., 2005)
Yeast *Saccharomyces cerevisae*	Interspecifc hybridization	(Smukowski Heil et al., 2021)
Yeast *Schizosaccharomyces pombe*	Environmental stress (heavy metals, caffeine, and the plasticizer phthalate)	(Esnault et al., 2019)
Yeast *Candida albicans*	Anti-fungal medication miconazole	(Zhu et al., 2014)
Fungal pathogen *Magnaporthe oryzae*	Heat shock, copper stress	(Chadha & Sharma, 2014)
Aspergillus oryzae	CuSO stress, heat shock for conidia (strong effect), acidic environment, oxidative stress, and UV irradiation (weak effect)	(Ogasawara et al., 2009)
Wheat fungal pathogen *Zymoseptoria tritici*	Nutrient starvation, host infection stress	(Fouché et al., 2020)
ALGAE		
Photosynthetic coral symbiont *Symbiodinium microadriaticum*	Heat stress	(Chen et al., 2018)
Diatom *Phaeodactylum tricornutum*	Nitrate limitation, exposure to diatom-derived reactive aldehydes that induce stress responses and cell death	(Maumus et al., 2009)
PLANTS		
Oats	Biotic and abiotic stresses, including UV light, wounding, salicylic acid, and fungal attack	(Chenais et al., 2012; Kimura et al., 2001; Pourrajab & Hekmatimoghaddam, 2021)
Wheat (*Triticum durum L.)*	Salt and light stress	(Woodrow et al., 2011)
Solanaceae	Stress, hormones	(Grandbastien et al., 2005; Grandbastien, 2015)
Solanum chilense	"Multiple stress-related signalling molecules"	(Salazar et al., 2007)
Tomato	Drought stress and abscisic acid signaling	(Benoit et al., 2019)
Tobacco, tomatoes	Low temperature	(Pourrajab & Hekmatimoghaddam, 2021)
Tobacco	Fungal attack	(Pourrajab & Hekmatimoghaddam, 2021)
Tobacco	Tissue culture growth, wounding and methyl jasmonate	(Hirochika, 1993; Takeda et al., 1998)
Tobacco	The toxic fungal elicitor cryptogein and reactive oxygen species	(Anca et al., 2014)

Table 15.2
(continued)

Brassica	Heat stress	(Pietzenuk et al. 2016)
Arabidopsis	Heat stress	(Cavrak et al., 2014; Ito et al., 2016; Masuda et al., 2017; Matsunaga et al., 2015) (Gaubert et al., 2017)
Arabidopsis	Tissue culture growth	(Steimer et al., 2000)
Arabidopsis	Autopolyploidy	(Baduel et al., 2019)
Antirrhinum majus	Low temperature	(Pourrajab & Hekmatimoghaddam, 2021)
Sunflowers	Interspecific hybridization	(Michalak, 2010)
Andropogoneae (maize and sorghum)	Polyploidy	(Ramachandran et al., 2020)
Rice	Hybridization with *Zizania*	(Wang et al., 2010)
Rice	Early embryo development, tissue culture growth, stresses of gamma-ray irradiation, and high hydrostatic pressure	(Hirochika et al., 1996; Teramoto et al., 2014)
Rice	Etoposide DNA damage	(Yang et al., 2012)
Maize	Roundup herbicide stress	(Tyczewska et al., 2021)
Maize	Viral infection	(Johns, Mottinger, & Freeling, 1985; Paszkowski, 2015)
METAZOA		
Nematode *Caenorhabditis elegans*	Heat shock (males only)	(Kurhanewicz et al., 2020)
Drosophila	Heat shock	(Jardim et al., 2015; Pereira et al., 2018)
Drosophila	Geographic isolation on volcanic islands and stresses from vulcanism	(Craddock, 2016)
Drosophila	Interspecific hybridization	(Carnelossi et al., 2014; Gámez-Visairas et al., 2020; Romero-Soriano et al., 2016; Romero-Soriano & Garcia Guerreiro, 2016)
Vertebrates		(Pappalardo et al., 2021)
Antarctic teleost *Trematomus*	Cold shock	(Auvinet et al., 2018)
Human cancer cells	Arsenic, mercury, chemotherapy	(Clapes et al., 2021; Habibi et al., 2014; Karimi et al., 2014)

memory of the last stress experienced (Avramova, 2015; Kinoshita & Seki, 2014). In other words, living organisms have the ability to rewrite and rewire their genomes when necessary. Rather than being the passive beneficiaries of random mutations and natural selection, all organisms play an active role in their own hereditary variation and evolution by activating transposable elements in response to ecological challenges. Because the newly mobilized elements will respond to the same stimulus that activated their original transposition, they can also serve as a molecular record of past traumas (Shapiro, 2011; Shapiro, 2013). That is why so many adaptive stress responses are linked to mobile DNA-derived CRMs (Butelli et al., 2012; Grandbastien, 2015; Lv et al., 2019; Makarevitch et al., 2015; Mao et al., 2015; Negi et al., 2016; Wang et al., 2017). In *Arabidopsis*, for example, a recent study found that mobile

DNA plays a role in responses to phosphate limitation, tolerance to high salt concentration, freezing temperatures, and arsenic toxicity (Joly-Lopez et al., 2017).

15.4 Conclusions about a Genomic and Biological View of Evolution

Free from the a priori need for a purely physicalist account of evolutionary change, we are able to elaborate a more sophisticated and complex biological description of how evolution works. That description is fully goal-oriented in nature. At the end of the eighteenth century, Erasmus Darwin (Charles' grandfather) defined the "three great objects of desire" for every living organism as "lust, hunger, and security" (E. Darwin, 1794). Today, we would phrase this as "the three goals of all life are survival, growth, and reproduction." Under normal circumstances in a relatively stable ecology, these goals are met by each species' inherited physiology, sensory systems, regulatory networks, and behavior. Under the unusual circumstances following ecological disruption, however, those inherited capabilities may prove inadequate to ensure survival, growth, and reproduction, which may require hereditary variation and adaptive innovation. In meeting such challenges, the organisms will activate transposable DNA elements as well as many other natural cell and genetic engineering capabilities, such as symbiogenesis (Kozo-Polyansky, 1924), mutagenic DNA repair (Al Mamun et al., 2012), and/or rapid widespread genome restructuring (Heng, 2019; Shapiro, 2021; Umbreit et al., 2020). Trying to cope with the new ecology, these diverse inherent biological mechanisms of genome variation can produce evolutionary changes that range from microevolutionary adaptations altering a small number of phenotypes to macroevolutionary transformations that alter genome structure and generate new species or even higher taxa with multiple phenotypic novelties (Goldschmidt, 1940; Heng, 2019). Only a small fraction of the more complex macroevolutionary changes will succeed, but those that do can be the founders of novel taxa displaying major adaptive innovations. Taxonomic and adaptive radiations after mass extinctions indicate that there is no single outcome for successful ecologically-triggered macroevolutionary changes (Ezcurra & Butler, 2018; Grossnickle, Smith, & Wilson, 2019; Magallón, Sánchez-Reyes, & Gómez-Acevedo, 2019; Soltis & Soltis, 2014). The survivors that give rise to major lineages must provide a novel basis for ongoing adaptive changes. In other words, mobile DNA elements and other biological engines of genome change constitute essential survival tools in a dynamic ecology, and that is why they are ubiquitous in living organisms.

There are several conclusions to draw from this purposive view of how evolutionary change occurs. First of all, punctuated equilibrium is the predicted pattern for origination of new life forms at episodes of maximal ecological disruption, such as those marked by mass extinctions (Gould, 1983). We can therefore interpret the discontinuous nature of the fossil record and the genomic record documenting transpositional bursts distinguishing closely related lineages (Belyayev, 2014; El Baidouri & Panaud, 2013) as evidence in favor of episodic self-modification as a primary mode of evolutionary change. Secondly, the active participation of sensory-regulated cellular functions generating novel DNA configurations in evolutionary transformations (tables 15.1 and 15.2) tells us that evolution is inherently biological and cannot be reduced to purely physical explanations, as Coyne and his fellow neo-Darwinians hoped. In particular, this teleological perspective involves the operation of biological cognition (i.e., sensory-based control and adaptative responses) to regulate the processes of genome modification (Regolin & Vallortigara, 2021; Shapiro, 2020).

Recognition of the cognitive aspect of the evolutionary process opens a range of hitherto forbidden questions for scientific exploration. For example, we know that mobile DNA elements and other change operations occur nonrandomly and can be targeted to specific genome locations, as they are in the vertebrate adaptive immune system (https://shapiro.bsd.uchicago.edu/ExtraRefs.TargetingNaturalGeneticEngineeringInGenome.shtml) (Asif-Laidin et al., 2020; Birchler & Presting, 2012; Buerstedde et al., 2014; Craigie & Bushman, 2014; Hickey et al., 2015; Parks et al., 2009). Based on knowledge of this targeting potential, we are now able to ask whether there is any demonstrable connection between the ecological challenge that activates transposition of mobile DNA elements and the choice of target insertion sites that may facilitate successful adaptation to that particular challenge. In bacteria, there are distinct mutational spectra for different stress conditions (Maharjan & Ferenci, 2015; Maharjan & Ferenci, 2017), the cells target multiple antibiotic resistance determinants to specialized genomic structures (Cambray et al., 2011; Guerin et al., 2009; Parks et al., 2009), and some molecular geneticists even claim to have evidence for "directed mutation" in the activation of specific functions by mobile DNA element insertions (Saier, Kukita, & Zhang, 2017). While these directed-mutation claims require further scrutiny, pursuing this kind of previously taboo question has the potential to uncover another layer of biological control over the evolutionary process, just as McClintock's unexpected discovery of transposable controlling elements did. Perhaps a deeper theoretical question is whether the capacity for actively and purposefully generating hereditary variation is an essential feature of life. It may well be the case that living organisms that are incapable of actively modifying their genomes would be doomed to extinction. If that inference turns out to be correct, then genome self-modification, or rewriting, would be another essential goal-oriented function to incorporate into our definition of what it means to be alive.

Notes

1. Even important neo-Darwinists agreed with this view of purposive action throughout biology (see P. A. Corning, quoting Theodosius Dobzhansky, in ch. 2 of this volume).

2. Darwin himself gave up on pure phyletic gradualism by the time he published his sixth edition of *The Origin*, where he wrote of "sports" or discrete "variations which seem to us in our ignorance to arise spontaneously. It appears that I formerly underrated the frequency and value of these latter forms of variation, as leading to permanent modifications of structure independently of natural selection" (Darwin, *The Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life, 6th ed.*, ch. 15, p. 395).

3. Note that the differences in numbers reflect the number of genomes sequenced for each taxon rather than any clear difference in propensity for forming such fusion proteins.

References

Al Mamun, A. A., M. J. Lombardo, C. Shee, A. M. Lisewski, C. Gonzalez, D. Lin, R. B. Nehring, C. Saint-Ruf, J. L. Gibson, R. L. Frisch, O. Lichtarge, P. J. Hastings, and S. M. Rosenberg. 2012. "Identity and Function of a Large Gene Network Underlying Mutagenic Repair of DNA Breaks." *Science* 338(6112):1344–1348.

Alioto, T., K. G. Alexiou, A. Bardil, F. Barteri, R. Castanera, F. Cruz, A. Dhingra, H. Duval, I. Martí Á Fernández, L. Frias, B. Galán, J. L. García, W. Howad, J. Gómez-Garrido, M. Gut, I. Julca, J. Morata, P. Puigdomènech, P. Ribeca, M. J. Rubio Cabetas, A. Vlasova, M. Wirthensohn, J. Garcia-Mas, T. Gabaldón, J. M. Casacuberta, and P. Arús. 2020. "Transposons Played a Major Role in the Diversification between the Closely Related Almond and Peach Genomes: Results from the Almond Genome Sequence." *Plant J* 101(2):455–472.

Anca, I. A., J. Fromentin, Q. T. Bui, C. Mhiri, M. A. Grandbastien, and F. Simon-Plas. 2014. "Different Tobacco Retrotransposons Are Specifically Modulated by the Elicitor Cryptogein and Reactive Oxygen Species." *J Plant Physiol* 171(16):1533–1540.

Anderson, E. 1954. “Hybridization as an Evolutionary Stimulus.” *Evolution* 8:378–388.

Asif-Laidin, A., C. Conesa, A. Bonnet, C. Grison, I. Adhya, R. Menouni, H. Fayol, N. Palmic, J. Acker, and P. Lesage. 2020. “A Small Targeting Domain in Ty1 Integrase Is Sufficient to Direct Retrotransposon Integration Upstream of Trna Genes.” *Embo J* 39(17):e104337.

Auvinet, J., P. Graca, L. Belkadi, L. Petit, E. Bonnivard, A. Dettai, W. H. Detrich, 3rd, C. Ozouf-Costaz, and D. Higuet. 2018. “Mobilization of Retrotransposons as a Cause of Chromosomal Diversification and Rapid Speciation: The Case for the Antarctic Teleost Genus Trematomus.” *BMC Genomics* 19(1):339.

Avramova, Z. 2015. “Transcriptional ‘Memory’ of a Stress: Transient Chromatin and Memory (Epigenetic) Marks at Stress-Response Genes.” *Plant J* 83(1):149–159.

Baduel, P., L. Quadrana, B. Hunter, K. Bomblies, and V. Colot. 2019. “Relaxed Purifying Selection in Autopolyploids Drives Transposable Element Over-Accumulation Which Provides Variants for Local Adaptation.” *Nat Commun* 10(1):5818.

Barbaglia, A. M., K. M. Klusman, J. Higgins, J. R. Shaw, L. C. Hannah, and S. K. Lal. 2012. “Gene Capture by Helitron Transposons Reshuffles the Transcriptome of Maize.” *Genetics* 190(3):965–975.

Batista, R. A., J. Moreno-Romero, Y. Qiu, J. van Boven, J. Santos-González, D. D. Figueiredo, and C. Köhler. 2019. “The Mads-Box Transcription Factor Pheres1 Controls Imprinting in the Endosperm by Binding to Domesticated Transposons.” *Elife* 8:e50541.

Baud, A., M. Wan, D. Nouaud, N. Francillonne, D. Anxolabéhère, and H. Quesneville. 2020. “Traces of Transposable Elements in Genome Dark Matter Coopted by Flowering Gene Regulation Networks.” *bioRxiv*.

Beadle, G. W. 1948. “The Genes of Men and Molds.” *Sci Am* 179(3):30–39.

Bejerano, G., C. B. Lowe, N. Ahituv, B. King, A. Siepel, S. R. Salama, E. M. Rubin, W. J. Kent, and D. Haussler. 2006. “A Distal Enhancer and an Ultraconserved Exon Are Derived from a Novel Retroposon.” *Nature* 441(7089):87–90.

Belyayev, A. 2014. “Bursts of Transposable Elements as an Evolutionary Driving Force.” *J Evol Biol* 27(12):2573–2584.

Bennetzen, J. L., and H. Wang. 2014. “The Contributions of Transposable Elements to the Structure, Function, and Evolution of Plant Genomes.” *Annu Rev Plant Biol* 65:505–530.

Benoit, M., H. G. Drost, M. Catoni, Q. Gouil, S. Lopez-Gomollon, D. Baulcombe, and J. Paszkowski. 2019. “Environmental and Epigenetic Regulation of Rider Retrotransposons in Tomato.” *PLoS Genet* 15(9):e1008370.

Birchler, J. A., and G. G. Presting. 2012. “Retrotransposon Insertion Targeting: A Mechanism for Homogenization of Centromere Sequences on Nonhomologous Chromosomes.” *Genes Dev* 26(7):638–640.

Bolotin, E., K. Chellappa, W. Hwang-Verslues, J. M. Schnabl, C. Yang, and F. M. Sladek. 2011. “Nuclear Receptor Hnf4alpha Binding Sequences Are Widespread in Alu Repeats.” *BMC Genomics* 12:560.

Bondos, S. E., and X. X. Tan. 2001. “Combinatorial Transcriptional Regulation: The Interaction of Transcription Factors and Cell Signaling Molecules with Homeodomain Proteins in Drosophila Development.” *Crit Rev Eukaryot Gene Expr* 11(1–3):145–171.

Bornholdt, S. 2001. “Modeling Genetic Networks and Their Evolution: A Complex Dynamical Systems Perspective.” *Biol Chem* 382(9):1289–1299.

Bourque, G., B. Leong, V. B. Vega, X. Chen, Y. L. Lee, K. G. Srinivasan, J. L. Chew, Y. Ruan, C. L. Wei, H. H. Ng, and E. T. Liu. 2008. “Evolution of the Mammalian Transcription Factor Binding Repertoire Via Transposable Elements.” *Genome Res* 18(11):1752–1762.

Bourque, G., K. H. Burns, M. Gehring, V. Gorbunova, A. Seluanov, M. Hammell, M. Imbeault, Z. Izsvak, H. L. Levin, T. S. Macfarlan, D. L. Mager, and C. Feschotte. 2018. “Ten Things You Should Know About Transposable Elements.” *Genome Biol* 19(1):199.

Bowman, J. L., L. N. Briginshaw, and S. N. Florent. 2019. “Evolution and Co-Option of Developmental Regulatory Networks in Early Land Plants.” *Curr Top Dev Biol* 131:35–53.

Bray, D. 2003. “Molecular Networks: The Top-Down View.” *Science* 301(5641):1864–1865.

Bray, D. 2009. *Wetware: A Computer in Every Living Cell*. New Haven, CT: Yale University Press.

Bray, D. 2012. “The Propagation of Allosteric States in Large Multiprotein Complexes.” *J Mol Biol* 425(9):1410–1414.

Bray, D. 2015. “Limits of Computational Biology.” *In Silico Biol* 12(1–2):1–7.

Bringaud, F., M. Muller, G. C. Cerqueira, M. Smith, A. Rochette, N. M. El-Sayed, B. Papadopoulou, and E. Ghedin. 2007. “Members of a Large Retroposon Family Are Determinants of Post-Transcriptional Gene Expression in Leishmania.” *PLoS Pathog* 3(9):1291–1307.

Buerstedde, J. M., J. Alinikula, H. Arakawa, J. J. McDonald, and D. G. Schatz. 2014. “Targeting of Somatic Hypermutation by Immunoglobulin Enhancer and Enhancer-Like Sequences.” *PLoS Biol* 12(4):e1001831.

Bukhari, A. I., J. A. Shapiro, and S. L. Adhya (Eds.). 1977. *DNA Insertion Elements, Plasmids and Episomes*. Cold Spring Harbor, NY: Cold Spring Harbor Press.

Butelli, E., C. Licciardello, Y. Zhang, J. Liu, S. Mackay, P. Bailey, G. Reforgiato-Recupero, and C. Martin. 2012. "Retrotransposons Control Fruit-Specific, Cold-Dependent Accumulation of Anthocyanins in Blood Oranges." *Plant Cell* 24(3):1242–1255.

Cambray, G., N. Sanchez-Alberola, S. Campoy, E. Guerin, S. Da Re, B. Gonzalez-Zorn, M. C. Ploy, J. Barbe, D. Mazel, and I. Erill. 2011. "Prevalence of Sos-Mediated Control of Integron Integrase Expression as an Adaptive Trait of Chromosomal and Mobile Integrons." *Mob DNA* 2(1):6.

Cao, C., J. Xu, G. Zheng, and X. G. Zhu. 2016. "Evidence for the Role of Transposons in the Recruitment of Cis-Regulatory Motifs During the Evolution of C4 Photosynthesis." *BMC Genomics* 17(1):201.

Carnelossi, E. A., E. Lerat, H. Henri, S. Martinez, C. M. Carareto, and C. Vieira. 2014. "Specific Activation of an I-Like Element in Drosophila Interspecific Hybrids." *Genome Biol Evol* 6(7):1806–1817.

Carotti, E., F. Carducci, A. Canapa, M. Barucca, S. Greco, M. Gerdol, and M. A. Biscotti. 2021. "Transposable Elements and Teleost Migratory Behaviour." *Int J Mol Sci* 22(2):602.

Castanera, R., L. Lopez-Varas, A. Borgognone, K. LaButti, A. Lapidus, J. Schmutz, J. Grimwood, G. Perez, A. G. Pisabarro, I. V. Grigoriev, J. E. Stajich, and L. Ramirez. 2016. "Transposable Elements Versus the Fungal Genome: Impact on Whole-Genome Architecture and Transcriptional Profiles." *PLoS Genet* 12(6):e1006108.

Cavrak, V. V., N. Lettner, S. Jamge, A. Kosarewicz, L. M. Bayer, and O. Mittelsten Scheid. 2014. "How a Retrotransposon Exploits the Plant's Heat Stress Response for Its Activation." *PLoS Genet* 10(1):e1004115.

Chadha, S. and M. Sharma. 2014. "Transposable Elements as Stress Adaptive Capacitors Induce Genomic Instability in Fungal Pathogen Magnaporthe Oryzae." *PLoS One* 9(4):e94415.

Chen, C., W. Wang, X. Wang, D. Shen, S. Wang, Y. Wang, B. Gao, K. Wimmers, J. Mao, K. Li, and C. Song. 2019. "Retrotransposons Evolution and Impact on Lncrna and Protein Coding Genes in Pigs." *Mob DNA* 10:19.

Chen, J. E., G. Cui, X. Wang, Y. J. Liew, and M. Aranda. 2018. "Recent Expansion of Heat-Activated Retrotransposons in the Coral Symbiont *Symbiodinium Microadriaticum*." *ISME J* 12(2):639–643.

Chenais, B., A. Caruso, S. Hiard, and N. Casse. 2012. "The Impact of Transposable Elements on Eukaryotic Genomes: From Genome Size Increase to Genetic Adaptation to Stressful Environments." *Gene* 509(1):7–15.

Chishima, T., J. Iwakiri, and M. Hamada. 2018. "Identification of Transposable Elements Contributing to Tissue-Specific Expression of Long Non-Coding RNAs." *Genes (Basel)* 9(1):23.

Chuong, E. B. 2013. "Retroviruses Facilitate the Rapid Evolution of the Mammalian Placenta." *Bioessays* 35(10):853–861.

Chuong, E. B. 2018. "The Placenta Goes Viral: Retroviruses Control Gene Expression in Pregnancy." *PLoS Biol* 16(10):e3000028.

Chuong, E. B., N. C. Elde, and C. Feschotte. 2016. "Regulatory Evolution of Innate Immunity through Co-Option of Endogenous Retroviruses." *Science* 351(6277):1083–1087.

Chuong, E. B. and C. Feschotte. 2013. "Evolution. Transposons up the Dosage." *Science* 342(6160):812–813.

Chuong, E. B., M. A. Rumi, M. J. Soares, and J. C. Baker. 2013. "Endogenous Retroviruses Function as Species-Specific Enhancer Elements in the Placenta." *Nat Genet* 45(3):325–329.

Clapes, T., A. Polyzou, P. Prater, Sagar, A. Morales-Hernández, M. G. Ferrarini, N. Kehrer, S. Lefkopoulos, V. Bergo, B. Hummel, N. Obier, D. Maticzka, A. Bridgeman, J. S. Herman, I. Ilik, L. Klaeylé, J. Rehwinkel, S. McKinney-Freeman, R. Backofen, A. Akhtar, N. Cabezas-Wallscheid, R. Sawarkar, R. Rebollo, D. Grün, and E. Trompouki. 2021. "Chemotherapy-Induced Transposable Elements Activate Mda5 to Enhance Haematopoietic Regeneration." *Nat Cell Biol* 23(7):704–717.

Corning, P. A. 2007. "Control Information Theory: The 'Missing Link' in the Science of Cybernetics." *Syst Res Behav Sci* 24(3):297–311.

Cosby, R. L., J. Judd, R. Zhang, A. Zhong, N. Garry, E. J. Pritham, and C. Feschotte. 2021. "Recurrent Evolution of Vertebrate Transcription Factors by Transposase Capture." *Science* 371(6531).

Craddock, E. M. 2016. "Profuse Evolutionary Diversification and Speciation on Volcanic Islands: Transposon Instability and Amplification Bursts Explain the Genetic Paradox." *Biol Direct* 11:44.

Craigie, R., and F. D. Bushman. 2014. "Host Factors in Retroviral Integration and the Selection of Integration Target Sites." *Microbiol Spectr* 2(6).

Cui, F., M. V. Sirotin, and V. B. Zhurkin. 2011. "Impact of Alu Repeats on the Evolution of Human P53 Binding Sites." *Biol Direct* 6(1):2.

Darwin, C. 1859. *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. London: John Russel.

Darwin, E. 1794. *Zoonomia; or, the Laws of Organic Life. Part I*. London: J. Johnson.

de Vries, H. 1905. *Species and Varieties, Their Origin by Mutation; Lectures Delivered at the University of California*. Chicago, IL: Open Court.

del Rosario, R. C., N. A. Rayan, and S. Prabhakar. 2014. "Noncoding Origins of Anthropoid Traits and a New Null Model of Transposon Functionalization." *Genome Res* 24(9):1469–1484.

Dunn-Fletcher, C. E., L. M. Muglia, M. Pavlicev, G. Wolf, M. A. Sun, Y. C. Hu, E. Huffman, S. Tumukuntala, K. Thiele, A. Mukherjee, S. Zoubovsky, X. Zhang, K. A. Swaggart, K. Y. B. Lamm, H. Jones, T. S. Macfarlan, and L. J. Muglia. 2018. "Anthropoid Primate-Specific Retroviral Element The1b Controls Expression of Crh in Placenta and Alters Gestation Length." *PLoS Biol* 16(9):e2006337.

Ecco, G., M. Cassano, A. Kauzlaric, J. Duc, A. Coluccio, S. Offner, M. Imbeault, H. M. Rowe, P. Turelli, and D. Trono. 2016. "Transposable Elements and Their Krab-Zfp Controllers Regulate Gene Expression in Adult Tissues." *Dev Cell* 36(6):611–623.

Ecco, G., M. Imbeault, and D. Trono. 2017. "Krab Zinc Finger Proteins." *Development* 144(15):2719–2729.

El Baidouri, M., and O. Panaud. 2013. "Comparative Genomic Paleontology across Plant Kingdom Reveals the Dynamics of Te-Driven Genome Evolution." *Genome Biol Evol* 5(5):954–965.

Elisaphenko, E. A., N. N. Kolesnikov, A. I. Shevchenko, I. B. Rogozin, T. B. Nesterova, N. Brockdorff, and S. M. Zakian. 2008. "A Dual Origin of the Xist Gene from a Protein-Coding Gene and a Set of Transposable Elements." *PLoS One* 3(6):e2521.

Ellison, C. and D. Bachtrog. 2019. "Recurrent Gene Co-Amplification on Drosophila X and Y Chromosomes." *PLoS Genet* 15(7):e1008251.

Ellison, C. E. and D. Bachtrog. 2013. "Dosage Compensation Via Transposable Element Mediated Rewiring of a Regulatory Network." *Science* 342(6160):846–850.

Emera, D., C. Casola, V. J. Lynch, D. E. Wildman, D. Agnew, and G. P. Wagner. 2012. "Convergent Evolution of Endometrial Prolactin Expression in Primates, Mice, and Elephants through the Independent Recruitment of Transposable Elements." *Mol Biol Evol* 29(1):239–247.

Esnault, C., M. Lee, C. Ham, and H. L. Levin. 2019. "Transposable Element Insertions in Fission Yeast Drive Adaptation to Environmental Stress." *Genome Res* 29(1):85–95.

Etchegaray, E., M. Naville, J. N. Volff, and Z. Haftek-Terreau. 2021. "Transposable Element-Derived Sequences in Vertebrate Development." *Mob DNA* 12(1):1.

Ezcurra, M. D., and R. J. Butler. 2018. "The Rise of the Ruling Reptiles and Ecosystem Recovery from the Permo-Triassic Mass Extinction." *Proc Biol Sci* 285(1880):20180361.

Ferrari, R., N. Grandi, E. Tramontano, and G. Dieci. 2021. "Retrotransposons as Drivers of Mammalian Brain Evolution." *Life (Basel)* 11(5).

Fouché, S., T. Badet, U. Oggenfuss, C. Plissonneau, C. S. Francisco, and D. Croll. 2020. "Stress-Driven Transposable Element De-Repression Dynamics and Virulence Evolution in a Fungal Pathogen." *Mol Biol Evol* 37(1):221–239.

Frank, J. A. and C. Feschotte. 2017. "Co-Option of Endogenous Viral Sequences for Host Cell Function." *Curr Opin Virol* 25:81–89.

Fu, B., H. Ma, and D. Liu. 2019. "Endogenous Retroviruses Function as Gene Expression Regulatory Elements During Mammalian Pre-Implantation Embryo Development." *Int J Mol Sci* 20(3).

Fu, H., W. Zhang, N. Li, J. Yang, X. Ye, C. Tian, X. Lu, and L. Liu. 2021. "Elevated Retrotransposon Activity and Genomic Instability in Primed Pluripotent Stem Cells." *Genome Biol* 22(1):201.

Gámez-Visairas, V., V. Romero-Soriano, J. Martí-Carreras, E. Segarra-Carrillo, and M. P. García Guerreiro. 2020. "Drosophila Interspecific Hybridization Causes a Deregulation of the Pirna Pathway Genes." *Genes (Basel)* 11(2).

Gaubert, H., D. H. Sanchez, H. G. Drost, and J. Paszkowski. 2017. "Developmental Restriction of Retrotransposition Activated in Arabidopsis by Environmental Stress." *Genetics* 207(2):813–821.

Goldschmidt, R. 1940/1982. *The Material Basis of Evolution, Reissued (the Silliman Memorial Lectures Series)*. New Haven, CT: Yale University Press.

Gould, S. J. 1983. "Punctuated Equilibrium and the Fossil Record." *Science* 219(4584):439–440.

Grandbastien, M. A. 2015. "Ltr Retrotransposons, Handy Hitchhikers of Plant Regulation and Stress Response." *Biochim Biophys Acta* 1849(4):403–416.

Grandbastien, M. A., C. Audeon, E. Bonnivard, J. M. Casacuberta, B. Chalhoub, A. P. Costa, Q. H. Le, D. Melayah, M. Petit, C. Poncet, S. M. Tam, M. A. Van Sluys, and C. Mhiri. 2005. "Stress Activation and Genomic Impact of Tnt1 Retrotransposons in Solanaceae." *Cytogenet Genome Res* 110(1–4):229–241.

Grossnickle, D. M., S. M. Smith, and G. P. Wilson. 2019. "Untangling the Multiple Ecological Radiations of Early Mammals." *Trends Ecol Evol* 34(10):936–949.

Grow, E. J., R. A. Flynn, S. L. Chavez, N. L. Bayless, M. Wossidlo, D. J. Wesche, L. Martin, C. B. Ware, C. A. Blish, H. Y. Chang, R. A. Pera, and J. Wysocka. 2015. "Intrinsic Retroviral Reactivation in Human Preimplantation Embryos and Pluripotent Cells." *Nature* 522(7555):221–225.

Guerin, E., G. Cambray, N. Sanchez-Alberola, S. Campoy, I. Erill, S. Da Re, B. Gonzalez-Zorn, J. Barbe, M. C. Ploy, and D. Mazel. 2009. "The Sos Response Controls Integron Recombination." *Science* 324(5930):1034.

Habibi, L., M. A. Shokrgozar, M. Tabrizi, M. H. Modarressi, and S. M. Akrami. 2014. "Mercury Specifically Induces Line-1 Activity in a Human Neuroblastoma Cell Line." *Mutat Res Genet Toxicol Environ Mutagen* 759:9–20.

Heng, H. H. 2008. "The Conflict between Complex Systems and Reductionism." *JAMA* 300(13):1580–1581.

Heng, H. H. 2019. *Genome Chaos: Rethinking Genetics, Evolution, and Molecular Medicine*: New York: Academic Press.

Hickey, A., C. Esnault, A. Majumdar, A. G. Chatterjee, J. R. Iben, P. G. McQueen, A. X. Yang, T. Mizuguchi, S. I. Grewal, and H. L. Levin. 2015. "Single-Nucleotide-Specific Targeting of the Tf1 Retrotransposon Promoted by the DNA-Binding Protein Sap1 of *Schizosaccharomyces Pombe*." *Genetics* 201(3):905–924.

Hirakawa, M., H. Nishihara, M. Kanehisa, and N. Okada. 2009. "Characterization and Evolutionary Landscape of Amnsine1 in Amniota Genomes." *Gene* 441(1–2):100–110.

Hirochika, H. 1993. "Activation of Tobacco Retrotransposons During Tissue Culture." *Embo J* 12(6):2521–2528.

Hirochika, H., K. Sugimoto, Y. Otsuki, H. Tsugawa, and M. Kanda. 1996. "Retrotransposons of Rice Involved in Mutations Induced by Tissue Culture." *Proc Natl Acad Sci U S A* 93(15):7783–7788.

Hou, J., D. Lu, A. S. Mason, B. Li, M. Xiao, S. An, and D. Fu. 2019. "Non-Coding RNAs and Transposable Elements in Plant Genomes: Emergence, Regulatory Mechanisms and Roles in Plant Development and Stress Responses." *Planta* 250(1):23–40.

Huda, A., N. J. Bowen, A. B. Conley, and I. K. Jordan. 2011a. "Epigenetic Regulation of Transposable Element Derived Human Gene Promoters." *Gene* 475(1):39–48.

Huda, A., E. Tyagi, L. Marino-Ramirez, N. J. Bowen, D. Jjingo, and I. K. Jordan. 2011b. "Prediction of Transposable Element Derived Enhancers Using Chromatin Modification Profiles." *PLoS One* 6(11):e27513.

Ito, H., J. M. Kim, W. Matsunaga, H. Saze, A. Matsui, T. A. Endo, Y. Harukawa, H. Takagi, H. Yaegashi, Y. Masuta, S. Masuda, J. Ishida, M. Tanaka, S. Takahashi, T. Morosawa, T. Toyoda, T. Kakutani, A. Kato, and M. Seki. 2016. "A Stress-Activated Transposon in Arabidopsis Induces Transgenerational Abscisic Acid Insensitivity." *Sci Rep* 6:23181.

Izsvak, Z., J. Wang, M. Singh, D. L. Mager, and L. D. Hurst. 2016. "Pluripotency and the Endogenous Retrovirus Hervh: Conflict or Serendipity?" *Bioessays* 38(1):109–117.

Jacob, F. and J. Monod. 1961. "Genetic Regulatory Mechanisms in the Synthesis of Proteins." *J Mol Biol* 3:318–356.

Jacques, P. E., J. Jeyakani, and G. Bourque. 2013. "The Majority of Primate-Specific Regulatory Sequences Are Derived from Transposable Elements." *PLoS Genet* 9(5):e1003504.

Jardim, S. S., A. P. Schuch, C. M. Pereira, and E. L. Loreto. 2015. "Effects of Heat and UV Radiation on the Mobilization of Transposon Mariner-Mos1." *Cell Stress Chaperones* 20(5):843–851.

Jjingo, D., A. Huda, M. Gundapuneni, L. Marino-Ramirez, and I. K. Jordan. 2011. "Effect of the Transposable Element Environment of Human Genes on Gene Length and Expression." *Genome Biol Evol* 3:259–271.

Johns, M. A., J. Mottinger, and M. Freeling. 1985. "A Low Copy Number, Copia-Like Transposon in Maize." *Embo J* 4(5):1093–1101.

Joly-Lopez, Z., E. Forczek, E. Vello, D. R. Hoen, A. Tomita, and T. E. Bureau. 2017. "Abiotic Stress Phenotypes Are Associated with Conserved Genes Derived from Transposable Elements." *Front Plant Sci* 8:2027.

Joly-Lopez, Z., D. R. Hoen, M. Blanchette, and T. E. Bureau. 2016. "Phylogenetic and Genomic Analyses Resolve the Origin of Important Plant Genes Derived from Transposable Elements." *Mol Biol Evol* 33(8):1937–1956.

Jordan, I. K., I. B. Rogozin, G. V. Glazko, and E. V. Koonin. 2003. "Origin of a Substantial Fraction of Human Regulatory Sequences from Transposable Elements." *Trends Genet* 19(2):68–72.

Jouffroy, O., S. Saha, L. Mueller, H. Quesneville, and F. Maumus. 2016. "Comprehensive Repeatome Annotation Reveals Strong Potential Impact of Repetitive Elements on Tomato Ripening." *BMC Genomics* 17(1):624.

Jurka, J., W. Bao, K. K. Kojima, O. Kohany, and M. G. Yurka. 2012. "Distinct Groups of Repetitive Families Preserved in Mammals Correspond to Different Periods of Regulatory Innovations in Vertebrates." *Biol Direct* 7(1):36.

Kannan, S., D. Chernikova, I. B. Rogozin, E. Poliakov, D. Managadze, E. V. Koonin, and L. Milanesi. 2015. "Transposable Element Insertions in Long Intergenic Non-Coding RNA Genes." *Front Bioeng Biotechnol* 3:71.

Karimi, A., Z. Madjd, L. Habibi, and S. M. Akrami. 2014. "Evaluating the Extent of Line-1 Mobility Following Exposure to Heavy Metals in Hepg2 Cells." *Biol Trace Elem Res* 160(1):143–151.

Kimura, Y., Y. Tosa, S. Shimada, R. Sogo, M. Kusaba, T. Sunaga, S. Betsuyaku, Y. Eto, H. Nakayashiki, and S. Mayama. 2001. "Oare-1, a Ty1-Copia Retrotransposon in Oat Activated by Abiotic and Biotic Stresses." *Plant Cell Physiol* 42(12):1345–1354.

Kinoshita, T., and M. Seki. 2014. "Epigenetic Memory for Stress Response and Adaptation in Plants." *Plant Cell Physiol* 55(11):1859–1863.

Kozo-Polyansky, B. M. 1924. *Symbiogenesis: A New Principle of Evolution*. (English translation by Victor Fet published 2010). Cambridge, MA: Harvard University Press.

Kunarso, G., N. Y. Chia, J. Jeyakani, C. Hwang, X. Lu, Y. S. Chan, H. H. Ng, and G. Bourque. 2010. "Transposable Elements Have Rewired the Core Regulatory Network of Human Embryonic Stem Cells." *Nat Genet* 42(7):631–634.

Kurhanewicz, N. A., D. Dinwiddie, Z. D. Bush, and D. E. Libuda. 2020. "Elevated Temperatures Cause Transposon-Associated DNA Damage in *C. elegans* Spermatocytes." *Curr Biol* 30(24):5007–5017 e5004.

Lamarck, J.-B. 1994. *Philosophie Zoologique, Original Edition of 1809 with Introduction by Andre Pichot*. Paris: Flammarion.

Lander, E. S., L. M. Linton, B. Birren, C. Nusbaum, M. C. Zody, J. Baldwin, K. Devon, K. Dewar, M. Doyle, W. FitzHugh, R. Funke, D. Gage, K. Harris, A. Heaford, J. Howland, L. Kann, J. Lehoczky, R. LeVine, P. McEwan, K. McKernan, J. Meldrim, J. P. Mesirov, C. Miranda, W. Morris, J. Naylor, C. Raymond, M. Rosetti, R. Santos, A. Sheridan, C. Sougnez, N. Stange-Thomann, N. Stojanovic, A. Subramanian, D. Wyman, J. Rogers, J. Sulston, R. Ainscough, S. Beck, D. Bentley, J. Burton, C. Clee, N. Carter, A. Coulson, R. Deadman, P. Deloukas, A. Dunham, I. Dunham, R. Durbin, L. French, D. Grafham, S. Gregory, T. Hubbard, S. Humphray, A. Hunt, M. Jones, C. Lloyd, A. McMurray, L. Matthews, S. Mercer, S. Milne, J. C. Mullikin, A. Mungall, R. Plumb, M. Ross, R. Shownkeen, S. Sims, R. H. Waterston, R. K. Wilson, L. W. Hillier, J. D. McPherson, M. A. Marra, E. R. Mardis, L. A. Fulton, A. T. Chinwalla, K. H. Pepin, W. R. Gish, S. L. Chissoe, M. C. Wendl, K. D. Delehaunty, T. L. Miner, A. Delehaunty, J. B. Kramer, L. L. Cook, R. S. Fulton, D. L. Johnson, P. J. Minx, S. W. Clifton, T. Hawkins, E. Branscomb, P. Predki, P. Richardson, S. Wenning, T. Slezak, N. Doggett, J. F. Cheng, A. Olsen, S. Lucas, C. Elkin, E. Uberbacher, M. Frazier, R. A. Gibbs, D. M. Muzny, S. E. Scherer, J. B. Bouck, E. J. Sodergren, K. C. Worley, C. M. Rives, J. H. Gorrell, M. L. Metzker, S. L. Naylor, R. S. Kucherlapati, D. L. Nelson, G. M. Weinstock, Y. Sakaki, A. Fujiyama, M. Hattori, T. Yada, A. Toyoda, T. Itoh, C. Kawagoe, H. Watanabe, Y. Totoki, T. Taylor, J. Weissenbach, R. Heilig, W. Saurin, F. Artiguenave, P. Brottier, T. Bruls, E. Pelletier, C. Robert, P. Wincker, D. R. Smith, L. Doucette-Stamm, M. Rubenfield, K. Weinstock, H. M. Lee, J. Dubois, A. Rosenthal, M. Platzer, G. Nyakatura, S. Taudien, A. Rump, H. Yang, J. Yu, J. Wang, G. Huang, J. Gu, L. Hood, L. Rowen, A. Madan, S. Qin, R. W. Davis, N. A. Federspiel, A. P. Abola, M. J. Proctor, R. M. Myers, J. Schmutz, M. Dickson, J. Grimwood, D. R. Cox, M. V. Olson, R. Kaul, C. Raymond, N. Shimizu, K. Kawasaki, S. Minoshima, G. A. Evans, M. Athanasiou, R. Schultz, B. A. Roe, F. Chen, H. Pan, J. Ramser, H. Lehrach, R. Reinhardt, W. R. McCombie, M. de la Bastide, N. Dedhia, H. Blocker, K. Hornischer, G. Nordsiek, R. Agarwala, L. Aravind, J. A. Bailey, A. Bateman, S. Batzoglou, E. Birney, P. Bork, D. G. Brown, C. B. Burge, L. Cerutti, H. C. Chen, D. Church, M. Clamp, R. R. Copley, T. Doerks, S. R. Eddy, E. E. Eichler, T. S. Furey, J. Galagan, J. G. Gilbert, C. Harmon, Y. Hayashizaki, D. Haussler, H. Hermjakob, K. Hokamp, W. Jang, L. S. Johnson, T. A. Jones, S. Kasif, A. Kaspryzk, S. Kennedy, W. J. Kent, P. Kitts, E. V. Koonin, I. Korf, D. Kulp, D. Lancet, T. M. Lowe, A. McLysaght, T. Mikkelsen, J. V. Moran, N. Mulder, V. J. Pollara, C. P. Ponting, G. Schuler, J. Schultz, G. Slater, A. F. Smit, E. Stupka, J. Szustakowski, D. Thierry-Mieg, J. Thierry-Mieg, L. Wagner, J. Wallis, R. Wheeler, A. Williams, Y. I. Wolf, K. H. Wolfe, S. P. Yang, R. F. Yeh, F. Collins, M. S. Guyer, J. Peterson, A. Felsenfeld, K. A. Wetterstrand, A. Patrinos, M. J. Morgan, P. de Jong, J. J. Catanese, K. Osoegawa, H. Shizuya, S. Choi, and Y. J. Chen. 2001. "Initial Sequencing and Analysis of the Human Genome." *Nature* 409(6822):860–921.

Lapp, H. E. and R. G. Hunter. 2016. "The Dynamic Genome: Transposons and Environmental Adaptation in the Nervous System." *Epigenomics* 8(2):237–249.

Lee, C., M. K. Bae, N. Choi, S. J. Lee, and S. J. Lee. 2021. "Genome Plasticity by Insertion Sequences Learned from a Case of Radiation-Resistant Bacterium *Deinococcus Geothermalis*." *Bioinform Biol Insights* 15:11779322211037437.

Lee, C., K. Choo, and S. J. Lee. 2020. "Active Transposition of Insertion Sequences by Oxidative Stress in *Deinococcus Geothermalis*." *Front Microbiol* 11:558747.

Lennartsson, A., E. Arner, M. Fagiolini, A. Saxena, R. Andersson, H. Takahashi, Y. Noro, J. Sng, A. Sandelin, T. K. Hensch, and P. Carninci. 2015. "Remodeling of Retrotransposon Elements During Epigenetic Induction of Adult Visual Cortical Plasticity by HDAC Inhibitors." *Epigenetics Chromatin* 8:55.

Lindblad-Toh, K., M. Garber, O. Zuk, M. F. Lin, B. J. Parker, S. Washietl, P. Kheradpour, J. Ernst, G. Jordan, E. Mauceli, L. D. Ward, C. B. Lowe, A. K. Holloway, M. Clamp, S. Gnerre, J. Alfoldi, K. Beal, J. Chang, H. Clawson, J. Cuff, F. Di Palma, S. Fitzgerald, P. Flicek, M. Guttman, M. J. Hubisz, D. B. Jaffe, I. Jungreis, W. J. Kent, D. Kostka, M. Lara, A. L. Martins, T. Massingham, I. Moltke, B. J. Raney, M. D. Rasmussen, J. Robinson, A. Stark, A. J. Vilella, J. Wen, X. Xie, M. C. Zody, J. Baldwin, T. Bloom, C. W. Chin, D. Heiman, R. Nicol, C. Nusbaum, S. Young, J. Wilkinson, K. C. Worley, C. L. Kovar, D. M. Muzny, R. A. Gibbs, A. Cree, H. H. Dihn, G. Fowler, S. Jhangiani, V. Joshi, S. Lee, L. R. Lewis, L. V. Nazareth, G. Okwuonu, J. Santibanez, W. C. Warren, E. R. Mardis,

G. M. Weinstock, R. K. Wilson, K. Delehaunty, D. Dooling, C. Fronik, L. Fulton, B. Fulton, T. Graves, P. Minx, E. Sodergren, E. Birney, E. H. Margulies, J. Herrero, E. D. Green, D. Haussler, A. Siepel, N. Goldman, K. S. Pollard, J. S. Pedersen, E. S. Lander, and M. Kellis. 2011. "A High-Resolution Map of Human Evolutionary Constraint Using 29 Mammals." *Nature* 478(7370):476–482.

Lisch, D. and J. L. Bennetzen. 2011. "Transposable Element Origins of Epigenetic Gene Regulation." *Curr Opin Plant Biol* 14(2):156–161.

Liu, M. and M. V. Eiden. 2011. "Role of Human Endogenous Retroviral Long Terminal Repeats (LTRs) in Maintaining the Integrity of the Human Germ Line." *Viruses* 3(6):901–905.

Lopes, F. R., D. Jjingo, C. R. da Silva, A. C. Andrade, P. Marraccini, J. B. Teixeira, M. F. Carazzolle, G. A. Pereira, L. F. Pereira, A. L. Vanzela, L. Wang, I. K. Jordan, and C. M. Cararetto. 2013. "Transcriptional Activity, Chromosomal Distribution and Expression Effects of Transposable Elements in Coffea Genomes." *PLoS One* 8(11):e78931.

Lowe, C. B., G. Bejerano, and D. Haussler. 2007. "Thousands of Human Mobile Element Fragments Undergo Strong Purifying Selection Near Developmental Genes." *Proc Natl Acad Sci U S A* 104(19):8005–8010.

Lowe, C. B., M. Kellis, A. Siepel, B. J. Raney, M. Clamp, S. R. Salama, D. M. Kingsley, K. Lindblad-Toh, and D. Haussler. 2011. "Three Periods of Regulatory Innovation During Vertebrate Evolution." *Science* 333(6045):1019–1024.

Lu, X., F. Sachs, L. Ramsay, P. E. Jacques, J. Goke, G. Bourque, and H. H. Ng. 2014. "The Retrovirus HERVH Is a Long Noncoding RNA Required for Human Embryonic Stem Cell Identity." *Nat Struct Mol Biol* 21(4):423–425.

Lv, Y., F. Hu, Y. Zhou, F. Wu, and B. S. Gaut. 2019. "Maize Transposable Elements Contribute to Long Non-Coding RNAs That Are Regulatory Hubs for Abiotic Stress Response." *BMC Genomics* 20(1):864.

Lynch, V. J., R. D. Leclerc, G. May, and G. P. Wagner. 2011. "Transposon-Mediated Rewiring of Gene Regulatory Networks Contributed to the Evolution of Pregnancy in Mammals." *Nat Genet* 43(11):1154–1159.

Lynch, V. J., M. C. Nnamani, A. Kapusta, K. Brayer, S. L. Plaza, E. C. Mazur, D. Emera, S. Z. Sheikh, F. Grutzner, S. Bauersachs, A. Graf, S. L. Young, J. D. Lieb, F. J. DeMayo, C. Feschotte, and G. P. Wagner. 2015. "Ancient Transposable Elements Transformed the Uterine Regulatory Landscape and Transcriptome During the Evolution of Mammalian Pregnancy." *Cell Rep* 10(4):551–561.

Lyon, M. F. 2000. "Line-1 Elements and X Chromosome Inactivation: A Function for 'Junk' DNA?" *Proc Natl Acad Sci U S A* 97(12):6248–6249.

Lyon, M. F. 2003. "The Lyon and the Line Hypothesis." *Semin Cell Dev Biol* 14(6):313–318.

Maezawa, S., A. Sakashita, M. Yukawa, X. Chen, K. Takahashi, K. G. Alavattam, I. Nakata, M. T. Weirauch, A. Barski, and S. H. Namekawa. 2020. "Super-Enhancer Switching Drives a Burst in Gene Expression at the Mitosis-to-Meiosis Transition." *Nat Struct Mol Biol* 27(10):978–988.

Magallón, S., L. L. Sánchez-Reyes, and S. L. Gómez-Acevedo. 2019. "Thirty Clues to the Exceptional Diversification of Flowering Plants." *Ann Bot* 123(3):491–503.

Maharjan, R., and T. Ferenci. 2015. "Mutational Signatures Indicative of Environmental Stress in Bacteria." *Mol Biol Evol* 32(2):380–391.

Maharjan, R. P., and T. Ferenci. 2017. "A Shifting Mutational Landscape in 6 Nutritional States: Stress-Induced Mutagenesis as a Series of Distinct Stress Input-Mutation Output Relationships." *PLoS Biol* 15(6):e2001477.

Makarevitch, I., A. J. Waters, P. T. West, M. Stitzer, C. N. Hirsch, J. Ross-Ibarra, and N. M. Springer. 2015. "Transposable Elements Contribute to Activation of Maize Genes in Response to Abiotic Stress." *PLoS Genet* 11(1):e1004915.

Mao, H., H. Wang, S. Liu, Z. Li, X. Yang, J. Yan, J. Li, L. S. Tran, and F. Qin. 2015. "A Transposable Element in a NAC Gene Is Associated with Drought Tolerance in Maize Seedlings." *Nat Commun* 6:8326.

Marino-Ramirez, L., K. C. Lewis, D. Landsman, and I. K. Jordan. 2005. "Transposable Elements Donate Lineage-Specific Regulatory Sequences to Host Genomes." *Cytogenet Genome Res* 110(1–4):333–341.

Maslowska, K. H., K. Makiela-Dzbenska, and I. J. Fijalkowska. 2019. "The SOS System: A Complex and Tightly Regulated Response to DNA Damage." *Environ Mol Mutagen* 60(4):368–384.

Masuda, S., K. Nozawa, W. Matsunaga, Y. Masuta, A. Kawabe, A. Kato, and H. Ito. 2017. "Characterization of a Heat-Activated Retrotransposon in Natural Accessions of Arabidopsis Thaliana." *Genes Genet Syst* 91(6):293–299.

Matsunaga, W., N. Ohama, N. Tanabe, Y. Masuta, S. Masuda, N. Mitani, K. Yamaguchi-Shinozaki, J. F. Ma, A. Kato, and H. Ito. 2015. "A Small RNA Mediated Regulation of a Stress-Activated Retrotransposon and the Tissue Specific Transposition During the Reproductive Period in *Arabidopsis*." *Front Plant Sci* 6:48.

Maumus, F., A. E. Allen, C. Mhiri, H. Hu, K. Jabbari, A. Vardi, M. A. Grandbastien, and C. Bowler. 2009. "Potential Impact of Stress Activated Retrotransposons on Genome Evolution in a Marine Diatom." *BMC Genomics* 10:624.

McClintock, B. 1950. "The Origin and Behavior of Mutable Loci in Maize." *Proc Natl Acad Sci U S A* 36(6):344–355.

McClintock, B. 1952. "Controlling Elements and the Gene." *Cold Spring Harb Symp Quant Biol* 21:197–216.

McClintock, B. 1984. "The Significance of Responses of the Genome to Challenge." *Science* 226(4676):792–801.

McClintock, B. 1987. *Discovery and Characterization of Transposable Elements: The Collected Papers of Barbara McClintock*. New York: Garland.

McEwen, G. K., D. K. Goode, H. J. Parker, A. Woolfe, H. Callaway, and G. Elgar. 2009. "Early Evolution of Conserved Regulatory Sequences Associated with Development in Vertebrates." *PLoS Genet* 5(12):e1000762.

Micale, L., M. N. Loviglio, M. Manzoni, C. Fusco, B. Augello, E. Migliavacca, G. Cotugno, E. Monti, G. Borsani, A. Reymond, and G. Merla. 2012. "A Fish-Specific Transposable Element Shapes the Repertoire of P53 Target Genes in Zebrafish." *PLoS One* 7(10):e46642.

Michalak, P. 2010. "An Eruption of Mobile Elements in Genomes of Hybrid Sunflowers." *Heredity (Edinb)* 104(4):329–330.

Mikkelsen, T. S., M. J. Wakefield, B. Aken, C. T. Amemiya, J. L. Chang, S. Duke, M. Garber, A. J. Gentles, L. Goodstadt, A. Heger, J. Jurka, M. Kamal, E. Mauceli, S. M. Searle, T. Sharpe, M. L. Baker, M. A. Batzer, P. V. Benos, K. Belov, M. Clamp, A. Cook, J. Cuff, R. Das, L. Davidow, J. E. Deakin, M. J. Fazzari, J. L. Glass, M. Grabherr, J. M. Greally, W. Gu, T. A. Hore, G. A. Huttley, M. Kleber, R. L. Jirtle, E. Koina, J. T. Lee, S. Mahony, M. A. Marra, R. D. Miller, R. D. Nicholls, M. Oda, A. T. Papenfuss, Z. E. Parra, D. D. Pollock, D. A. Ray, J. E. Schein, T. P. Speed, K. Thompson, J. L. VandeBerg, C. M. Wade, J. A. Walker, P. D. Waters, C. Webber, J. R. Weidman, X. Xie, M. C. Zody, J. A. Graves, C. P. Ponting, M. Breen, P. B. Samollow, E. S. Lander, and K. Lindblad-Toh. 2007. "Genome of the Marsupial *Monodelphis Domestica* Reveals Innovation in Non-Coding Sequences." *Nature* 447(7141):167–177.

Muino, J. M., S. de Bruijn, A. Pajoro, K. Geuten, M. Vingron, G. C. Angenent, and K. Kaufmann. 2016. "Evolution of DNA-Binding Sites of a Floral Master Regulatory Transcription Factor." *Mol Biol Evol* 33(1):185–200.

Mulholland, C. B., A. Nishiyama, J. Ryan, R. Nakamura, M. Yiğit, I. M. Glück, C. Trummer, W. Qin, M. D. Bartoschek, F. R. Traube, E. Parsa, E. Ugur, M. Modic, A. Acharya, P. Stolz, C. Ziegenhain, M. Wierer, W. Enard, T. Carell, D. C. Lamb, H. Takeda, M. Nakanishi, S. Bultmann, and H. Leonhardt. 2020. "Recent Evolution of a TET-Controlled and DPPA3/STELLA-Driven Pathway of Passive DNA Demethylation in Mammals." *Nat Commun* 11(1):5972.

Nakanishi, A., N. Kobayashi, A. Suzuki-Hirano, H. Nishihara, T. Sasaki, M. Hirakawa, K. Sumiyama, T. Shimogori, and N. Okada. 2012. "A Sine-Derived Element Constitutes a Unique Modular Enhancer for Mammalian Diencephalic Fgf8." *PLoS One* 7(8):e43785.

Naville, M., I. A. Warren, Z. Haftek-Terreau, D. Chalopin, F. Brunet, P. Levin, D. Galiana, and J. N. Volff. 2016. "Not So Bad after All: Retroviruses and Long Terminal Repeat Retrotransposons as a Source of New Genes in Vertebrates." *Clin Microbiol Infect* 22(4):312–323.

Negi, P., A. N. Rai, and P. Suprasanna. 2016. "Moving through the Stressed Genome: Emerging Regulatory Roles for Transposons in Plant Stress Response." *Front Plant Sci* 7:1448.

Nishihara, H. 2019. "Retrotransposons Spread Potential Cis-Regulatory Elements During Mammary Gland Evolution." *Nucleic Acids Res* 47(22):11551–11562.

Nishihara, H. 2020. "Transposable Elements as Genetic Accelerators of Evolution: Contribution to Genome Size, Gene Regulatory Network Rewiring and Morphological Innovation." *Genes Genet Syst* 94(6):269–281.

Nishihara, H., N. Kobayashi, C. Kimura-Yoshida, K. Yan, O. Bormuth, Q. Ding, A. Nakanishi, T. Sasaki, M. Hirakawa, K. Sumiyama, Y. Furuta, V. Tarabykin, I. Matsuo, and N. Okada. 2016. "Coordinately Co-Opted Multiple Transposable Elements Constitute an Enhancer for *wnt5a* Expression in the Mammalian Secondary Palate." *PLoS Genet* 12(10):e1006380.

Notwell, J. H., T. Chung, W. Heavner, and G. Bejerano. 2015. "A Family of Transposable Elements Co-Opted into Developmental Enhancers in the Mouse Neocortex." *Nat Commun* 6:6644.

Ogasawara, H., H. Obata, Y. Hata, S. Takahashi, and K. Gomi. 2009. "Crawler, a Novel Tc1/Mariner-Type Transposable Element in *Aspergillus Oryzae* Transposes under Stress Conditions." *Fungal Genet Biol* 46(6–7):441–449.

Okada, N., T. Sasaki, T. Shimogori, and H. Nishihara. 2010. "Emergence of Mammals by Emergency: Exaptation." *Genes Cells* 15(8):801–812.

Oliver, M. J., O. Schofield, and K. Bidle. 2010. "Density Dependent Expression of a Diatom Retrotransposon." *Mar Genomics* 3(3–4):145–150.

Pal, C., K. Asiani, S. Arya, C. Rensing, D. J. Stekel, D. G. J. Larsson, and J. L. Hobman. 2017. "Metal Resistance and Its Association with Antibiotic Resistance." *Adv Microb Physiol* 70:261–313.

Pappalardo, A. M., V. Ferrito, M. A. Biscotti, A. Canapa, and T. Capriglione. 2021. "Transposable Elements and Stress in Vertebrates: An Overview." *Int J Mol Sci* 22(4).

Parks, A. R., Z. Li, Q. Shi, R. M. Owens, M. M. Jin, and J. E. Peters. 2009. "Transposition into Replicating DNA Occurs through Interaction with the Processivity Factor." *Cell* 138(4):685–695.

Paszkowski, J. 2015. "Controlled Activation of Retrotransposition for Plant Breeding." *Curr Opin Biotechnol* 32:200–206.

Pattee, H. H. (Ed.). 1973. *Hierarchy Theory: The Challenge of Complex Systems*. New York: Braziller.

Pauls, S., D. K. Goode, L. Petrone, P. Oliveri, and G. Elgar. 2015. "Evolution of Lineage-Specific Functions in Ancient Cis-Regulatory Modules." *Open Biol* 5(11):150079.

Pereira, C. M., T. J. R. Stoffel, S. M. Callegari-Jacques, A. Hua-Van, P. Capy, and E. L. S. Loreto. 2018. "The Somatic Mobilization of Transposable Element Mariner-Mos1 During the Drosophila Lifespan and Its Biological Consequences." *Gene* 679:65–72.

Pezzulo, G. and M. Levin. 2016. "Top-Down Models in Biology: Explanation and Control of Complex Living Systems above the Molecular Level." *J R Soc Interface* 13(124).

Pietzenuk, B., C. Markus, H. Gaubert, N. Bagwan, A. Merotto, E. Bucher, and A. Pecinka. 2016. "Recurrent Evolution of Heat-Responsiveness in *Brassicaceae Copia* Elements." *Genome Biol* 17(1):209.

Piskurek, O. and D. J. Jackson. 2012. "Transposable Elements: From DNA Parasites to Architects of Metazoan Evolution." *Genes (Basel)* 3(3):409–422.

Pittendrigh, C. S. 1958. *Adaptation, Natural Selection, and Behavior*, edited by A. Roe and George Gaylord Simpson. New Haven, CT: Yale University Press.

Polak, P., and E. Domany. 2006. "Alu Elements Contain Many Binding Sites for Transcription Factors and May Play a Role in Regulation of Developmental Processes." *BMC Genomics* 7:133.

Polavarapu, N., L. Mariño-Ramírez, D. Landsman, J. F. McDonald, and I. K. Jordan. 2008. "Evolutionary Rates and Patterns for Human Transcription Factor Binding Sites Derived from Repetitive DNA." *BMC Genomics* 9:226.

Policarpi, C., L. Crepaldi, E. Brookes, J. Nitarska, S. M. French, A. Coatti, and A. Riccio. 2017. "Enhancer SINEs Link Pol Iii to Pol Ii Transcription in Neurons." *Cell Rep* 21(10):2879–2894.

Polychronopoulos, D., J. W. D. King, A. J. Nash, G. Tan, and B. Lenhard. 2017. "Conserved Non-Coding Elements: Developmental Gene Regulation Meets Genome Organization." *Nucleic Acids Res* 45(22):12611–12624.

Pourrajab, F. and S. Hekmatimoghaddam. 2021. "Transposable Elements, Contributors in the Evolution of Organisms (from an Arms Race to a Source of Raw Materials)." *Heliyon* 7(1):e06029.

Qiu, Y., and C. Köhler. 2020. "Mobility Connects: Transposable Elements Wire New Transcriptional Networks by Transferring Transcription Factor Binding Motifs." *Biochem Soc Trans* 48(3):1005–1017.

Ramachandran, D., M. R. McKain, E. A. Kellogg, and J. S. Hawkins. 2020. "Evolutionary Dynamics of Transposable Elements Following a Shared Polyploidization Event in the Tribe Andropogoneae." *G3 (Bethesda)* 10(12):4387–4398.

Rebeiz, M., N. H. Patel, and V. F. Hinman. 2015. "Unraveling the Tangled Skein: The Evolution of Transcriptional Regulatory Networks in Development." *Annu Rev Genomics Hum Genet* 16:103–131.

Rebollo, R., M. T. Romanish, and D. L. Mager. 2012. "Transposable Elements: An Abundant and Natural Source of Regulatory Sequences for Host Genes." *Annu Rev Genet* 46:21–42.

Regolin, L., and G. Vallortigara. 2021. "Rethinking Cognition: From Animal to Minimal." *Biochem Biophys Res Commun* 564:1–3.

Reznikoff, W. S. 1992. "The Lactose Operon-Controlling Elements: A Complex Paradigm." *Mol Microbiol* 6(17):2419–2422.

Riegler, A. 2008. "Natural or Internal Selection? The Case of Canalization in Complex Evolutionary Systems." *Artif Life* 14(3):345–362.

Rishishwar, L., L. Wang, J. Wang, S. V. Yi, J. Lachance, and I. K. Jordan. 2018. "Evidence for Positive Selection on Recent Human Transposable Element Insertions." *Gene* 675:69–79.

Roman, A. C., F. J. Gonzalez-Rico, and P. M. Fernandez-Salguero. 2011a. "B1-SINE Retrotransposons: Establishing Genomic Insulatory Networks." *Mob Genet Elements* 1(1):66–70.

Roman, A. C., F. J. Gonzalez-Rico, E. Molto, H. Hernando, A. Neto, C. Vicente-Garcia, E. Ballestar, J. L. Gomez-Skarmeta, J. Vavrova-Anderson, R. J. White, L. Montoliu, and P. M. Fernandez-Salguero. 2011b. "Dioxin Receptor and Slug Transcription Factors Regulate the Insulator Activity of B1 SINE Retrotransposons Via an RNA Polymerase Switch." *Genome Res* 21(3):422–432.

Römer, C., M. Singh, L. D. Hurst, and Z. Izsvák. 2017. "How to Tame an Endogenous Retrovirus: HERVH and the Evolution of Human Pluripotency." *Curr Opin Virol* 25:49–58.

Romero-Soriano, V., N. Burlet, D. Vela, A. Fontdevila, C. Vieira, and M. P. Garcia Guerreiro. 2016. "Drosophila Females Undergo Genome Expansion after Interspecific Hybridization." *Genome Biol Evol* 8(3):556–561.

Romero-Soriano, V. and M. P. Garcia Guerreiro. 2016. "Expression of the Retrotransposon Helena Reveals a Complex Pattern of TE Deregulation in Drosophila Hybrids." *PLoS One* 11(1):e0147903.

Saber, M. M., I. Adeyemi Babarinde, N. Hettiarachchi, and N. Saitou. 2016. "Emergence and Evolution of Hominidae-Specific Coding and Noncoding Genomic Sequences." *Genome Biol Evol* 8(7):2076–2092.

Sacerdot, C., G. Mercier, A. L. Todeschini, M. Dutreix, M. Springer, and P. Lesage. 2005. "Impact of Ionizing Radiation on the Life Cycle of Saccharomyces Cerevisiae Ty1 Retrotransposon." *Yeast* 22(6):441–455.

Saier, M. H., Jr., C. Kukita, and Z. Zhang. 2017. "Transposon-Mediated Directed Mutation in Bacteria and Eukaryotes." *Front Biosci (Landmark Ed)* 22:1458–1468.

Sakashita, A., S. Maezawa, K. Takahashi, K. G. Alavattam, M. Yukawa, Y. C. Hu, S. Kojima, N. F. Parrish, A. Barski, M. Pavlicev, and S. H. Namekawa. 2020. "Endogenous Retroviruses Drive Species-Specific Germline Transcriptomes in Mammals." *Nat Struct Mol Biol* 27(10):967–977.

Sakurai, T., S. Nakagawa, H. Bai, R. Bai, K. Kusama, A. Ideta, Y. Aoyagi, K. Kaneko, K. Iga, J. Yasuda, T. Miyazawa, and K. Imakawa. 2017. "Novel Endogenous Retrovirus-Derived Transcript Expressed in the Bovine Placenta Is Regulated by WNT Signaling." *Biochem J* 474(20):3499–3512.

Salazar, M., E. González, J. A. Casaretto, J. M. Casacuberta, and S. Ruiz-Lara. 2007. "The Promoter of the TLC1.1 Retrotransposon from *Solanum chilense* Is Activated by Multiple Stress-Related Signaling Molecules." *Plant Cell Rep* 26(10):1861–1868.

Salces-Ortiz, J., C. Vargas-Chavez, L. Guio, G. E. Rech, and J. González. 2020. "Transposable Elements Contribute to the Genomic Response to Insecticides in *Drosophila Melanogaster*." *Philos Trans R Soc Lond B Biol Sci* 375(1795):20190341.

Santangelo, A. M., F. S. de Souza, L. F. Franchini, V. F. Bumaschny, M. J. Low, and M. Rubinstein. 2007. "Ancient Exaptation of a Core-Sine Retroposon into a Highly Conserved Mammalian Neuronal Enhancer of the Proopiomelanocortin Gene." *PLoS Genet* 3(10):1813–1826.

Santoni, F. A., J. Guerra, and J. Luban. 2012. "HERV-H RNA Is Abundant in Human Embryonic Stem Cells and a Precise Marker for Pluripotency." *Retrovirology* 9:111.

Sasaki, T., H. Nishihara, M. Hirakawa, K. Fujimura, M. Tanaka, N. Kokubo, C. Kimura-Yoshida, I. Matsuo, K. Sumiyama, N. Saitou, T. Shimogori, and N. Okada. 2008. "Possible Involvement of SINEs in Mammalian-Specific Brain Formation." *Proc Natl Acad Sci U S A* 105(11):4220–4225.

Schwarzer, W., and F. Spitz. 2014. "The Architecture of Gene Expression: Integrating Dispersed Cis-Regulatory Modules into Coherent Regulatory Domains." *Curr Opin Genet Dev* 27:74–82.

Servant, G., C. Pennetier, and P. Lesage. 2008. "Remodeling Yeast Gene Transcription by Activating the Ty1 Long Terminal Repeat Retrotransposon under Severe Adenine Deficiency." *Mol Cell Biol* 28(17):5543–5554.

Sexton, C. E., R. L. Tillett, and M. V. Han. 2021. "The Essential but Enigmatic Regulatory Role of HERVH in Pluripotency." *Trends Genet* 38(1):12–21.

Shapiro, J., and D. Noble. 2021. "What Prevents Mainstream Evolutionists Teaching the Whole Truth About How Genomes Evolve?" *Prog Biophys Mol Biol* 165:140–152.

Shapiro, J. A. 1983. *Mobile Genetic Elements*. New York: Academic Press.

Shapiro, J. A. 2011. *Evolution: A View from the 21st Century*. Upper Saddle River, NJ: FT Press Science.

Shapiro, J. A. 2013. "How Life Changes Itself: The Read-Write (RW) Genome." *Phys Life Rev* 10(3):287–323.

Shapiro, J. A. 2017. "Living Organisms Author Their Read-Write Genomes in Evolution." *Biology (Basel)* 6(4):42.

Shapiro, J. A. 2019. "No Genome Is an Island: Toward a 21st Century Agenda for Evolution." *Ann NY Acad Sci* 1447(1):21–52.

Shapiro, J. A. 2020. "All Living Cells Are Cognitive." *Biochem Biophys Res Commun* 564:134–149.

Shapiro, J. A. 2021. "What Can Evolutionary Biology Learn from Cancer Biology?" *Prog Biophys Mol Biol* 165:19–28.

Shapiro, J. A. 2022. *Evolution: A View from the 21st Century. Fortified*, 2nd ed. Chicago: Cognition Press.

Smukowski Heil, C., K. Patterson, A. S. Hickey, E. Alcantara, and M. J. Dunham. 2021. "Transposable Element Mobilization in Interspecific Yeast Hybrids." *Genome Biol Evol* 13(3):evab033.

Soltis, P. S., and D. E. Soltis. 2014. "Flower Diversity and Angiosperm Diversification." *Methods Mol Biol* 1110:85–102.

Spirov, A. V., E. A. Zagriychuk, and D. M. Holloway. 2014. "Evolutionary Design of Gene Networks: Forced Evolution by Genomic Parasites." *Parallel Process Lett* 24(2).

Sprague Jr., G. F. 1991. "Signal Transduction in Yeast Mating: Receptors, Transcription Factors, and the Kinase Connection." *Trends Genet* 7(11–12):393–398.

Srinivasachar Badarinarayan, S., and D. Sauter. 2021. "Switching Sides: How Endogenous Retroviruses Protect Us from Viral Infections." *J Virol* 95(12):e02299–20.

Stebbins, Jr., G. L. 1951. "Cataclysmic Evolution." *Scientific American* 184(4):54–59.

Steimer, A., P. Amedeo, K. Afsar, P. Fransz, O. Mittelsten Scheid, and J. Paszkowski. 2000. "Endogenous Targets of Transcriptional Gene Silencing in Arabidopsis." *Plant Cell* 12(7):1165–1178.

Sun, M. A., G. Wolf, Y. Wang, A. D. Senft, S. Ralls, J. Jin, C. E. Dunn-Fletcher, L. J. Muglia, and T. S. Macfarlan. 2021. "Endogenous Retroviruses Drive Lineage-Specific Regulatory Evolution across Primate and Rodent Placentae." *Mol Biol Evol* 38(11):4992–5004.

Sundaram, V., Y. Cheng, Z. Ma, D. Li, X. Xing, P. Edge, M. P. Snyder, and T. Wang. 2014. "Widespread Contribution of Transposable Elements to the Innovation of Gene Regulatory Networks." *Genome Res* 24(12):1963–1976.

Suryamohan, K., and M. S. Halfon. 2015. "Identifying Transcriptional Cis-Regulatory Modules in Animal Genomes." *Wiley Interdiscip Rev Dev Biol* 4(2):59–84.

Suzuki, H., T. Taketani, M. Tanabiki, M. Ohara, J. Kobayashi, and T. Ohshiro. 2021. "Frequent Transposition of Multiple Insertion Sequences in Geobacillus Kaustophilus Hta426." *Front Microbiol* 12:650461.

Takeda, S., K. Sugimoto, H. Otsuki, and H. Hirochika. 1998. "Transcriptional Activation of the Tobacco Retrotransposon Tto1 by Wounding and Methyl Jasmonate." *Plant Mol Biol* 36(3):365–376.

Tashiro, K., A. Teissier, N. Kobayashi, A. Nakanishi, T. Sasaki, K. Yan, V. Tarabykin, L. Vigier, K. Sumiyama, M. Hirakawa, H. Nishihara, A. Pierani, and N. Okada. 2011. "A Mammalian Conserved Element Derived from SINE Displays Enhancer Properties Recapitulating Satb2 Expression in Early-Born Callosal Projection Neurons." *PLoS One* 6(12):e28497.

Teramoto, S., T. Tsukiyama, Y. Okumoto, and T. Tanisaka. 2014. "Early Embryogenesis-Specific Expression of the Rice Transposon *Ping* Enhances Amplification of the MITE *mPing*." *PLoS Genet* 10(6):e1004396.

Testori, A., L. Caizzi, S. Cutrupi, O. Friard, M. De Bortoli, D. Cora, and M. Caselle. 2012. "The Role of Transposable Elements in Shaping the Combinatorial Interaction of Transcription Factors." *BMC Genomics* 13(1):400.

Todeschini, A. L., A. Morillon, M. Springer, and P. Lesage. 2005. "Severe Adenine Starvation Activates Ty1 Transcription and Retrotransposition in *Saccharomyces Cerevisiae*." *Mol Cell Biol* 25(17):7459–7472.

Torres-Padilla, M. E. 2020. "On Transposons and Totipotency." *Philos Trans R Soc Lond B Biol Sci* 375(1795):20190339.

Toussaint, M., and W. von Seelen. 2007. "Complex Adaptation and System Structure." *Biosystems* 90(3):769–782.

Trizzino, M., Y. Park, M. Holsbach-Beltrame, K. Aracena, K. Mika, M. Caliskan, G. H. Perry, V. J. Lynch, and C. D. Brown. 2017. "Transposable Elements Are the Primary Source of Novelty in Primate Gene Regulation." *Genome Res* 27(10):1623–1633.

Tyczewska, A., J. Gracz-Bernaciak, J. Szymkowiak, and T. Twardowski. 2021. "Herbicide Stress-Induced DNA Methylation Changes in Two Zea Mays Inbred Lines Differing in Roundup® Resistance." *J Appl Genet* 62(2):235–248.

Umbreit, N. T., C. Z. Zhang, L. D. Lynch, L. J. Blaine, A. M. Cheng, R. Tourdot, L. Sun, H. F. Almubarak, K. Judge, T. J. Mitchell, A. Spektor, and D. Pellman. 2020. "Mechanisms Generating Cancer Genome Complexity from a Single Cell Division Error." *Science* 368(6488):eaba0712.

van de Lagemaat, L. N., J. R. Landry, D. L. Mager, and P. Medstrand. 2003. "Transposable Elements in Mammals Promote Regulatory Variation and Diversification of Genes with Specialized Functions." *Trends Genet* 19(10): 530–536.

Vandecraen, J., P. Monsieurs, M. Mergeay, N. Leys, A. Aertsen, and R. Van Houdt. 2016. "Zinc-Induced Transposition of Insertion Sequence Elements Contributes to Increased Adaptability of *Cupriavidus metallidurans*." *Front Microbiol* 7:359.

Vicient, C. M., and J. M. Casacuberta. 2017. "Impact of Transposable Elements on Polyploid Plant Genomes." *Ann Bot* 120(2):195–207.

Volff, J. N. 2006. "Turning Junk into Gold: Domestication of Transposable Elements and the Creation of New Genes in Eukaryotes." *Bioessays* 28(9):913–922.

Voronova, A., M. Rendón-Anaya, P. Ingvarsson, R. Kalendar, and D. Ruņģis. 2020. "Comparative Study of Pine Reference Genomes Reveals Transposable Element Interconnected Gene Networks." *Genes (Basel)* 11(10):1216.

Wang, D., Z. Qu, L. Yang, Q. Zhang, Z. H. Liu, T. Do, D. L. Adelson, Z. Y. Wang, I. Searle, and J. K. Zhu. 2017. "Transposable Elements (TEs) Contribute to Stress-Related Long Intergenic Noncoding RNAs in Plants." *Plant J* 90(1):133–146.

Wang, J., N. J. Bowen, L. Marino-Ramirez, and I. K. Jordan. 2009. "A c-Myc Regulatory Subnetwork from Human Transposable Element Sequences." *Mol Biosyst* 5(12):1831–1839.

Wang, J., C. Vicente-Garcia, D. Seruggia, E. Molto, A. Fernandez-Minan, A. Neto, E. Lee, J. L. Gomez-Skarmeta, L. Montoliu, V. V. Lunyak, and I. K. Jordan. 2015. "MIR Retrotransposon Sequences Provide Insulators to the Human Genome." *Proc Natl Acad Sci U S A* 112(32):4428–4437.

Wang, J., G. Xie, M. Singh, A. T. Ghanbarian, T. Raskó, A. Szvetnik, H. Cai, D. Besser, A. Prigione, N. V. Fuchs, G. G. Schumann, W. Chen, M. C. Lorincz, Z. Ivics, L. D. Hurst, and Z. Izsvák. 2014. "Primate-Specific Endogenous Retrovirus-Driven Transcription Defines Naive-Like Stem Cells." *Nature* 516(7531):405–409.

Wang, N., H. Wang, H. Wang, D. Zhang, Y. Wu, X. Ou, S. Liu, Z. Dong, and B. Liu. 2010. "Transpositional Reactivation of the *Dart* Transposon Family in Rice Lines Derived from Introgressive Hybridization with *Zizania Latifolia*." *BMC Plant Biol* 10:190.

Wang, X., G. Ai, C. Zhang, L. Cui, J. Wang, H. Li, J. Zhang, and Z. Ye. 2016. "Expression and Diversification Analysis Reveals Transposable Elements Play Important Roles in the Origin of Lycopersicon-Specific lncRNAs in Tomato." *New Phytol* 209(4):1442–1455.

Warren, I. A., M. Naville, D. Chalopin, P. Levin, C. S. Berger, D. Galiana, and J. N. Volff. 2015. "Evolutionary Impact of Transposable Elements on Genomic Diversity and Lineage-Specific Innovation in Vertebrates." *Chromosome Res* 23(3):505–531.

Wiener, N. 1965. *Cybernetics or Control and Communication in the Animal and the Machine*. Cambridge, MA: MIT Press.

Woodrow, P., G. Pontecorvo, L. F. Ciarmiello, A. Fuggi, and P. Carillo. 2011. "Ttd1a Promoter Is Involved in DNA-Protein Binding by Salt and Light Stresses." *Mol Biol Rep* 38(6):3787–3794.

Woolfe, A., and G. Elgar. 2008. "Organization of Conserved Elements near Key Developmental Regulators in Vertebrate Genomes." *Adv Genet* 61:307–338.

Xiang, Y., and H. Liang. 2021. "The Regulation and Functions of Endogenous Retrovirus in Embryo Development and Stem Cell Differentiation." *Stem Cells Int* 2021:6660936.

Yang, X., Y. Yu, L. Jiang, X. Lin, C. Zhang, X. Ou, K. Osabe, and B. Liu. 2012. "Changes in DNA Methylation and Transgenerational Mobilization of a Transposable Element (*mPing*) by the Topoisomerase II Inhibitor, Etoposide, in Rice." *BMC Plant Biol* 12:48.

Zhang, X., and L. J. Muglia. 2021. "Baby's Best Foe-Riend: Endogenous Retroviruses and the Evolution of Eutherian Reproduction." *Placenta* 113:1–7.

Zhang, Y. D., Z. Chen, Y. Q. Song, C. Liu, and Y. P. Chen. 2005. "Making a Tooth: Growth Factors, Transcription Factors, and Stem Cells." *Cell Res* 15(5):301–316.

Zhao, H., W. Zhang, L. Chen, L. Wang, A. P. Marand, Y. Wu, and J. Jiang. 2018. "Proliferation of Regulatory DNA Elements Derived from Transposable Elements in the Maize Genome." *Plant Physiol* 176(4):2789–2803.

Zhu, C. X., L. Yan, X. J. Wang, Q. Miao, X. X. Li, F. Yang, Y. B. Cao, P. H. Gao, X. L. Bi, and Y. Y. Jiang. 2014. "Transposition of the Zorro2 Retrotransposon Is Activated by Miconazole in *Candida albicans*." *Biol Pharm Bull* 37(1):37–43.