Transposable elements in eukaryotic genomes: epigenetic regulation by the host and functionalization for the host.

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Transposable elements (TEs), including retrotransposons and DNA transposons, are mutagenic elements that occupy a substantial fraction of their host genomes. Because an unrestricted activity of TEs greatly reduces the host fitness, their transpositional activity must be tightly regulated at the levels of transcription, translation, and transposition. In eukaryotes, one of the host defense systems against TEs is epigenetic silencing by DNA methylation and posttranslational chemical modifications of histones. Indeed, it has been proposed that the epigenetic regulatory system emerged as a defense system against TEs, and subsequently expanded to the control of endogenous genes. Recently, accumulating evidence have indicated that a specific set of small RNAs, siRNAs in plants and piRNAs in animals, constitutes another molecular mechanism of the host defense. These small RNAs not only induce digestion of TE mRNAs but also guide chromatin-mediated transcriptional silencing, highlighting the reinforcing interaction between these silencing mechanisms. One of the recent hot topics is that TE-derived small RNAs produced in germ cells are inherited to progenies and convey the phenotype of the parent, which is resistance to TEs, in a non-Mendelian manner. In this issue of *Genes and Genetic Systems*, Ito and Saito provide reviews on recent findings about the biogenesis, function, and inheritance of the TE-derived small RNAs in plants and animals.

When Dr. Barbara McClintock discovered TEs and called them “controlling elements” in 1950’s, the importance of TEs in the function and evolution of the genome was not appropriately recognized. Rather, they were long regarded as selfish DNAs. Later, however, it was uncovered that TEs constitute a large fraction of eukaryotic genomes (more than a half in some cases), and that

some copies of TEs regulate genes. Today, it is undoubted that TEs play important roles in eukaryotic biology. In some cases, TE sequences gave rise to new proteins that benefit the hosts, such as RAG1 involved in antibody diversity, Peg10 in placental organogenesis, and SASPase in skin hydration. For the role of TEs in gene regulation, SINE retrotransposons are of particular interest because of their enormous copy numbers (>1,000,000 copies per mammalian genome) and their tendency to reside within and close to genes; for example, if you work on a human gene, you would find tens of *Alu* SINEs in introns of your gene. Despite their shortness (less than 500 bp long), many SINEs carry regulatory sequences. In the following review article, I will discuss on the roles for SINEs in regulation of gene expression, and how these SINE functions are regulated epigenetically.

I underscore that the epigenetic regulatory system does not kill or remove TEs. It just keeps the transpositional activity at low levels and minimizes the influence of TEs present at respective genomic locations. This allows generation of genetic, and possibly epigenetic, diversity in the host population. Soon or long after transposition, the host would occasionally take advantage of opportunities to utilize TEs for rewiring the regulatory network or inventing new important proteins. With the power of massive DNA sequencers, genomic and epigenomic studies continue to reveal the genetic and epigenetic interactions between TEs and the other parts of the genome. I would like to close introductory remarks with a foresighted description made more than half a century ago. — *Gene elements and controlling elements represent two different classes of primary components of chromosome and a close relationship exists between them.* (McClintock, B., 1956, *Cold Spring Harb Symp Quant Biol.* 21:197-216)