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Custom RNA-Seq methods identify tissue- and age-specific patterns of retrotransposon expression in vivo.

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Retrotransposons have been continuously amplifying in mammalian genomes through a copy-and-paste mechanism. This has allowed them to produce millions of copies that represent >30 percent of their host genome. Transposon-associated genomic alterations have contributed to genome diversity and evolution. Germ-line and somatic retrotransposition of Long Interspersed Element-1 (LINE-1, L1) and Short Interspersed Element (SINE) have caused a broad spectrum of diseases. In the brain, LINE-1 mobilization has been suggested to contribute to neuronal plasticity suggesting its potential to influence behavioral traits.

LINE-1 amplification begins with transcription involving the use of the element's internal promoter to produce LINE-1 mRNAs. Until recently it has been impossible to determine which of the few thousands of full-length L1 loci are expressed and how their expression patterns change with age and may be altered by genetic defects or external stimuli. This is because conventional techniques are unable to accurately measure expression of retrotransposons that occurs exclusively from their own promoter. This knowledge is important for understanding tissue-specific susceptibility to L1 damage in vivo. Therefore, we have developed NGS-based methods that detect mRNA expression from individual L1 loci in human cells and tissues from model organisms. These approaches show that the subsets of expressed L1 loci are cell-type and tissue-specific and that L1 mRNA expression changes with age in a tissue-specific manner as well as in response to external stimuli. We have also developed custom animal models of L1 retrotransposition that show that both genetic defects and external stimuli can affect L1 mobilization in vivo.