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## Molecular Features of Endogenous Retrovirus in Humans

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The human endogenous retroviruses (HERVs) have been subjected to many amplification and transposition events resulting in a widespread distribution of complete or partial retroviral sequences throughout the human genome. Expression of HERVs can influence the outcome of infections in different ways that can be either beneficial or detrimental to the host. A function of the multiple copy families, scattered throughout the genome, has been reported regulatory functions on the gene expression of nearby located genes. The vast majority of these have no influence on gene function or relevance to pathology. A small minority of such sequences has acquired a role in regulating gene expression, and some of these may be related to differences between individuals, and to expression of disease. HERV insertion event during primate evolution could be genetic marker for the study of phylogeny and evolution. The HERV elements have formation of an RNA transcript that must then be reverse-transcribed and inserted into a new location in the genome. Most important regulatory gene sequences reside in the LTR elements that contain the binding sites for host cell factors. The integrated proviral or LTR elements could evolve new biological functions during primate evolution, and regulate transcriptional potential. Expression of those elements varied significantly among cell lines, in some cases showing strict cell type specificity. Accumulated changes of the LTR elements in gene regulation are likely to be functional factors for the process of diversification, speciation and evolution consequences. Implication of the HERV elements in human diseases results from immune disturbance, recombination excision, altering gene structure, and abnormal expression.

**Keywords:** HERV elements; gene expression, LTRs, evolution and phylogeny, primates

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## Cocaine-associated Neuronal Plasticity in the Striatum

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Activation of metabotropic glutamate receptors (mGluRs) in striatal GABA neurons couples glutamatergic signals to the second messengers in a subtype-specific manner. For instance, stimulation of group I mGluRs upregulates $Ca^{2+}$ cascades, while group II/III downregulates adenylate cyclase and cAMP cascades. Dominant presynaptic inhibitory actions of the group II/III mGluRs on glutamate release, desensitization of the group I mGluRs in response to prolonged stimulation of glutamate, and extensive cross-talks between protein kinases by various second messengers downstream to the mGluRs have been documented. In addition to the spatiotemporal processes, interactions of glutamate receptors and protein phosphatase activities against protein kinase actions further regulate glutamatergic signals in the striatum. Using a novel type of glutamate microbiosensor, our research group has been monitored the changes of extracellular glutamate levels in the dorsal striatum by repeated cocaine administration. In addition, alterations of the phosphorylation of NMDA and AMPA receptor subunits by cocaine-induced activation of the group I mGluRs have been observed. The results demonstrated that repeated cocaine significantly increased the levels of extracellular glutamate in the dorsal striatum. Parallel with these data, the immunoreactivity of phosphorylated glutamate receptor subunits by repeated cocaine was increased through group I mGluR-dependent activation of protein kinases in the dorsal striatum. In this presentation, thus, putative mechanisms underlying cocaine-induced neuronal plasticity will be further discussed.

**Key words:** Drugs of abuse, glutamate receptor, biosensor, protein kinase, dorsal striatum