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Bioinformatic Application of Retroviral Elements in Cancer and Primates

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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. Most HERVs seem to have entered the genome between 30 and 50 million years ago, and they comprise over 200 distinct groups and subgroups. At least 22 independent HERV families within human genome have been reported, suggesting the presence of those retroviral families within the 8% of the human genome. Most of them were highly defective with large deletions, stop codons, and frameshifts in the open reading frames. However, structural genes from some HERV families are expressed preferentially in human placenta and several cancer cell lines. 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. They have extremely effective promoters, enhancers, polyadenylation signals, and transcription factor binding sites. Most important regulatory gene sequences surely reside in the LTR elements that contain the binding sites for host cell factors. Functional LTR transcription start sites are located between the R and U5 region (3′ termini of the R region). Accumulated changes of the LTR elements in gene regulation are likely to be functional factors for the process of diversification, speciation and evolution consequences. 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. They seemed to be a source of structural change of genomes, and could be related to genetic variation connected with diseases. Therefore, they have been proposed as etiological cofactors in chronic diseases such as cancer and neurological disease. The HERV elements have also been implicated in other diseases such as male infertility, type I diabetes mellitus, psoriatic and atopic dermatitis skin, seminoma. Most of studies of the pathological potential of HERVs have looked

for expression of HERV RNA or protein, on the assumption that disease symptoms result from inflammatory of autoimmune reactions to HERV proteins. The effect of HERVs in disease may be at the level of cellular gene transcription, however, since it is well known that enhancer and promoter elements in retroviral LTRs, which can influence the transcription of neighboring genes. Taken together, implication of the HERV elements in human diseases results from immune disturbance, recombination excision, altering gene structure, and abnormal expression. To summary, the HERVs and solitary LTR elements have contributed in genomic plasticity during primate evolution, indicating that they could be genetic marker for understanding evolutionary history. They have involved in the diversification, speciation and evolution consequences including induction and progression of several diseases by genomic disturbance and regulation. The HERV elements could create new functional exons by integration and adaption events and express in specific tissues by LTR alternative promoter. Elucidation of various roles of the HERVs and solitary LTR elements deserves continuous investigation for understanding hominid evolution and diseases.

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