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„Characterization of the *NWC* gene promoter activity in selected vertebrate species”

Abstract

The *RAG-1* and *RAG-2* genes (recombination-activating genes) encode subunits of a V(D)J recombinase responsible for rearrangements of antibody and T cell receptor genes. It is widely accepted that the presence of *RAG* genes in the genomes of jawed vertebrates and other lineages is a result of the integration of a DNA transposon. While a substantial amount of evidence that clarifies the nature of the *RAG* transposon has been gathered, far less attention has been paid to the genomic site of its integration in various host organisms. To avoid epigenetic inactivation, the DNA transposons integrate into sites that have a high transcription activating potential, including sites near genes controlled by bidirectional promoters. In all genomes of the jawed vertebrates that have been studied to date, the *RAG* genes are located in close proximity to the *NWC* gene. The aim of the study was to characterize the promoter of the *NWC* gene and to determine whether it has a bidirectional activity and whether it is an evolutionarily conserved feature.

The obtained results indicate the evolutionary conservation of the features of the structure and functioning of the *NWC* promoter between the studied species of *M. musculus*, *H. sapiens*, *X. tropicalis* and *D. rerio*, including: a control over head-to-head oriented genes, a size less than 1600 bp, a presence of a CpG island, a presence of a Zfp143 transcription factor recognition sites, an activation of the promoter by binding of the Zfp143 factor and the bidirectional activity. The conclusion based on the gathered information is that the bidirectional activity of the *NWC* promoter could have occurred in the common ancestor of the jawed vertebrates and that the location of *RAG* genes in the *NWC locus* is a direct outcome of the transposon integration in that site. Obtained results support the hypothesis which postulates multiple integrations of the *RAG* transposon during the evolution of Deuterostomes. On the basis of the results obtained in this study and other data an attempt of reconstruction of the evolutionary development of the mechanisms that control the transcription in the *RAG/NWC locus* was made. The constitutive bidirectional activity of *NWC* promoter could be the factor that enabled integration of the *RAG* transposon into the *NWC gene locus* and helped to avoid its epigenetic silencing, which let the *RAG* genes to undertake their currently known function.