Phylogenetic Analysis of the p53 Family

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Abstract—A relationship between the functional significance of individual amino acid residues of p53, their positions in the protein structure, and the mode of the evolution of the codons corresponding to these residues was established. A phylogenetic analysis of the coding sequences of the gene of p53 from 32 vertebrate species was performed. It was found that directional selection affects the codons influencing the efficiency of binding of p53 as a transcription factor to DNA. It was shown that, in conserved codons, the frequency of generative mutations maintaining the normal function of the protein statistically reliably differs from the frequency of mutations with the effects of loss and acquisition of function and the dominant negative effect. The phylogenetic analysis and molecular dynamics simulations also confirmed the functional significance of the residue G245, for which the formation of a Zn^{2+}-binding site in the G245C substitution was previously assumed.

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