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■4794■ Identification of p53 target sequences by network parallel computing.

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p53 is a transcription factor that specifically recognizes DNA sequences containing two adjacent copies of the consensus sequences. p53 activates the expression of substantial number of genes important for cell cycle regulation and apoptosis, through binding to the DNA-binding sites. Identification of transcriptional targets of p53 is of great importance in understanding the pathways by which p53 regulates growth arrest and apoptosis. We have developed a web-based genome-wide analyzing system on DNA motifs using network multi-parallel computing. The system allowed us to explore the binding sites of a gene regulatory protein, p53, which gene is the most important one in human cancer. Our system consists of three components; 1) web server which presents user interface, 2) task controller which issues control commands to data processing nodes, and 3) parallel computing engines. Our system predicted known p53 binding sites with 100% accuracy. We examined all p53 binding sites through whole genome by this system. Total number of binding sequences on human genome is 3000 when only sequences that match all 20 base pairs to the consensus sequences. Expression analysis of putative target genes in p53 wild type mouse embryonic fibroblasts (MEF) and p53^{-/-}-MEF revealed that xx and xx express in p53 dependent manner. Luciferase activity using the constructs that contain p53 binding sequences showed the presence of transcription activity in these sequences. These results indicated that in silico approach to identify p53 target genes through p53 consensus sequences greatly reduce labor and time consuming step. The information of genes containing p53 consensus binding sequence in the regulatory region will greatly assist the identification of p53 target genes, which could be potential targets for cancer chemotherapeutic drugs.

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