Artificial Transcription Factors Based on Zinc Finger Motifs toward Gene Regulation and Analysis

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Regulation of a target gene at will is one of the most prospective themes in the post-genomic era. An artificial transcription factor with desired DNA binding specificity could work as a powerful tool to control target genes. In this presentation, I will talk about creation and function of artificial C_2H_2-type zinc finger proteins. The zinc finger motif is one of the most typical DNA binding motifs found in a lot of transcription factors. The motif has attractive characteristics to create novel DNA binding proteins from following points, (1) recognition of 3 base pairs per motif, (2) mediation of base recognitions by specific amino acids, (3) a DNA binding module consistent of tandemly repeated zinc finger motifs, and (4) binding to non-palindromic sequence. Novel DNA recognition patterns can be obtained through replacement of amino acids that involve in DNA recognition. By connecting multiple zinc finger motifs, a long DNA sequence can be recognized. In addition, DNA sequence-specific function can be given by fusing a zinc finger domain and an effecter domain with transcriptional activation/repression or DNA cleavage functions. I have exchanged the connection region (linker) between zinc finger motifs to various linkers. It is suggested that the components and the structure of a linker play an important role to determine the DNA binding selectivity and function though linker itself dose not contribute to direct DNA base recognition. I will also discuss possibility of artificial zinc finger proteins as a new tool for gene regulation and analysis.