GS3-1 Artificial transcription factors based on multi-zinc finger motifs

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Artificial transcription factors targeting any desired genes are very attractive from the standpoint of regulating biological functions. In order to generate such transcription factors, specific DNA binding domains are required to address a single site for each gene promoter. C_2H_2 type zinc finger motif is one of the best frameworks to create new artificial DNA binding proteins for the following features: the zinc finger motif can recognize three bases DNA, be tandemly repeated by covalent linkage, and work as a monomer. Manifold zinc finger proteins targeting various DNA sequences have been created so far. For application to a target in sequences as complex as the human genome, the significantly strict specificity in DNA binding must be required. We, therefore, designed a new zinc finger protein by fusing 9 motifs (multi-zinc finger protein), and created an artificial transcription factor containing it as a DNA binding domain. We extensively observed the kinetics of the transcriptional activation *in cellulo*. As a result we found that the multi-zinc finger type artificial transcription factor activates the reporter gene promptly when cells contain the transcription factor above a certain amount of it. On the other hand, significant delay on the onset time of transcriptional activation is observed depending on the decrease in the amount of the transcription factor. Taking advantage of this fact, it could be possible to control the onset time of activation or repression of a target gene. It suggests the great potential of artificial transcription factors based on multi-zinc finger motifs as a tool for gene therapy.