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RNA cleavage activity of DNA enzyme and Hammerhead ribozyme targeted to TEL/AML1 fusion gene

Ki-Ryeon Seol[1], Soo-Jung Gong[2] and Dong-Eun Kim[1,2]

[1]Department of Biomaterial Control and [2]Department of Biotechnology and Bioengineering, Dong-Eui University, Busan 614-714, Korea.

Acute lymphoblastic leukemia (ALL) results from chromosomal translocation between chromosomes 12 and 21, which creates TEL/AML1 fusion gene. The fusion gene encodes abnormal mRNA that is translated to the chimeric protein, TEL/AML1. TEL/AML1 contains the first 336 amino acids of TEL that is linked to residues 21-480 of AML1 and the fusion protein was known as a transcription repressor to various target genes. In order to repress the expression of TEL/AML1 gene in human erythroleukemia cells, we first synthesized several RNA-cleaving antisense oligonucleotides, such as DNA enzyme and hammerhead ribozyme, which are targeted against TEL/AML1 junction. We have *in vitro* synthesized TEL/AML1 mRNA fragment containing junction of two genes, TEL and AML1, as a RNA substrate for these RNA-cleaving catalytic nucleic acids. Three DNA enzymes and one hammerhead ribozyme were designed to recognize and cleave different parts of TEL/AML1 mRNA substrate, all of which specifically bind to the junction of the two genes. These catalytic antisense oligonucleotides were *in vitro* compared in target RNA cleavage activity. One of the DNA enzymes and the hammerhead ribozyme demonstrated their efficient RNA-cleavage activity *in vitro*. Especially, the hammerhead ribozyme exhibited RNA-cleavage activity in a multiple turnover kinetics regime. Thus, both the hammerhead ribozyme and the DNAzyme targeted TEL/AML1 fusion mRNA will be potentially useful as gene-inactivating agents in the treatment of leukemia, such as ALL.