Abstract

In recent years, more and more attention has been paid to gene therapy. To provide targets and methods for gene therapy, we introduced the screening method of exonic lncRNA, the mechanism of lencRNA *PRKDC-210* and the feasibility of Double duplex invasion DNA for gene therapy in this paper.

In recent years, long noncoding RNAs (lncRNAs) have received increasing attention and have been reported to be associated with various genetic abnormalities. However, the functions of many lncRNAs, including those of long exonic noncoding RNAs (lencRNAs), have not yet been elucidated. Here, we used a novel tethering luciferase assay to analyze the transcriptional regulatory functions of five lencRNAs that are upregulated in cancer. We found that the lencRNA PRKDC-210 interacts with MED12, a component of the CDK8 complex, to regulate the transcription of several genes. The transcriptional activation ability of PRKDC-210 was abolished in siRNA-treated CDK8-depleted cells. We also confirmed the enrichment of PRKDC-210 on RNA polymerase II. RNA-seq analysis of cells in which PRKDC-210 or PRKDC mRNA was knocked down using antisense oligonucleotides revealed that PRKDC-210 can affect the expression levels of genes related to fatty acid metabolism. Finally, we used a ChIRP assay to examine PRKDC-210-enriched sites in the genome. Overall, our findings demonstrate that the lencRNA PRKDC-210 promotes transcription through the CDK8 complex pathway at the transcription initiation site. We propose that PRKDC-210 can affect the transcription of adjacent genes after its transcription and splicing.

Cancer is the deadliest disease now. Although there is a lot of research on cancer treatment, cancer is still difficult to cure. Here, we show a new anti gene that could be used for cancer treatment. Anti gene (double duplex invasion DNA) was developed by Fujimoto Lab in JAIST. This is a photo-cross-linking oligonucleotide toward the target gene by induction at 385 nm UV irradiation. To assess its potential in cancer treatment, we investigated the effect of this anti gene on cells. The EGFP gene was used as a target gene to evaluate the effect of the anti gene in cells. Because it's easier to observe. We used an EGFP stable expressing HeLa cell line in this study. The viability of cells after anti gene activation was confirmed by MTT assay. To assess apoptosis, the contents of caspase-3 and cleaved caspase-3 were detected by western blotting. We detected a large amount of caspase-3 and cleaved caspase-3 in the cells treated with anti gene. This proves that anti gene triggered apoptosis. Collectively, double duplex invasion DNA must be activated by 385nm UV radiation to photo-cross-linking with the target gene and trigger apoptosis. I think we can use this anti gene to target cancer-specific genes and use UV to control its activation. In this way, we can kill cancer cells and cause less damage to normal cells.

Keyword: lncRNA, transcriptional regulation, gene therapy, anti gene