Gene Regulation and Therapeutic Potential of Inverted Alu Repeats

Yoosik Kim

Department of Chemical and Biomolecular Engineering,
Korea Advanced Institute of Science and Technology, Republic of Korea

Alu elements are ~300 nucleotides long transposable elements found abundantly in primate genomes. With more than 1.1 million copies, they occupy more than 10% of our genome. Interestingly, the Alu elements are found primarily on noncoding parts of gene-rich regions, such as introns and UTRs, rather than randomly distributed throughout the genome. When two inverted repeats of Alu elements (IRAlus) are located in the 3' UTR, the resulting long double-stranded RNA (dsRNA) structure leads to sequestration in nuclear paraspeckles and subsequent translational suppression of the host mRNA. Despite this additive post-transcriptional regulatory layer, the physiological function of gene silencing by 3′ UTR IRAlus remains unknown.

Our laboratory investigates the regulation and biological significance of gene regulation by IRAlus. To elucidate the genes that are potentially regulated by IRAlus, we employ high-throughput sequencing to identify all dsRNA regulatory elements existing in 3′ UTRs. Furthermore, we utilize RNA interference to modulate the length of the 3′ UTR to study the downstream effect of IRAlus regulatory elements. We find that IRAlus may play a significant role during tumorigenesis as well as in neurodegenerative diseases. Moreover, the expression of IRAlus can be exploited to enhance the therapeutic effects of anti-mitotic drugs. In this presentation, we discuss our recent efforts in studying gene regulation by IRAlus and their significance in the pathogenesis of human diseases.