Gene Regulation by Alu Elements in Untranslated Regions

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Abstract

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, Alu elements are found primarily on noncoding parts of gene-rich regions, such as introns and UTRs. When two inverted Alu repeats (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 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 the development of 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 pathological significance and therapeutic potential.

Biography

Dr. Yoosik Kim is a chemical and biological engineering Ph.D. graduate from Princeton University, and studied signal transduction cascades in early embryos. Post-Ph.D., he delved into RNA biology and studied the innate immune regulation by cellular double-stranded RNAs (dsRNAs) at Seoul National University. He became a professor in the Department of Chemical and Biomolecular Engineering at KAIST in 2016, studying the regulation and function of cellular double-stranded RNAs (dsRNAs). Originally identified in viruses, dsRNAs are recognized by innate immune sensors and trigger inflammatory responses in cells. Notably, the human genome encodes various repeat elements that can generate cellular dsRNAs. Dr. Kim’s lab employs molecular biology, biochemistry, and bioinformatics to understand how cellular dsRNAs are regulated, their interaction with RNA-binding proteins, and their implications in inflammatory diseases.