第4回 疾患エピゲノムコアセンターセミナー

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Epitranscrioptome Sequencing Technologies: Decoding RNA Modifications

More than 100 different types of post-transcriptional modifications to RNA molecules have been characterized so far. Modifications in non-coding RNAs greatly impact their biological functions and have been extensively studied. In contrast, our knowledge regarding to the prevalence, mechanism and function of chemical modifications to mRNA and long non-coding RNA is limited. Because many RNA modifications form regular base pairs during reverse transcription and are of very low abundance, highly selective and sensitive methods with low background are required for their detection. In my lab, we utilize selective chemical/biochemical labeling to develop high throughput sequencing methods for these RNA modifications; in particular, we have developed two specific technologies for the transcriptome-wide sequencing of pseudouridine (Ψ) and N1-methyladenosine in RNA, respectively. With CeU-Seq, we identified thousands of Ψ sites in human cells and mouse tissues, showed that hPUS1 acts on mRNA and revealed inducible and stress-specific mRNA pseudouridylation events. With m1A-ID-Seq, we identified ~900 m1A peaks in mRNA and ncRNA, revealed a prominent feature of enrichment in the 5'-untranslated region of mRNA transcripts and demonstrated that m1A in mRNA is reversible by hALKBH3, a known RNA/DNA demethylase. Such transcriptome-wide sequencing technologies will allow future functional studies of these RNA modifications.

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