Lecture Code : BR01-S3
Session Name : Basic Research
Session Topic : Gene Therapy / RNA Therapy
Date & Time, Place : June 20 (Fri) / 08:30-10:30 / Room 1 (GBR 101)

Epitranscriptomics in Kidney Disease: Insights and Therapeutic Potential

SZUYUAN LI
Taipei Veterans General Hospital, Taiwan, Taiwan

Epitranscriptomics is an emerging field in molecular biology focused on the study of chemical modifications of RNA molecules, particularly after transcription. Unlike classic genetics, which considers the DNA sequence, epitranscriptomics emphasizes how RNA modifications influence gene expression, stability, and function. One significant modification is N6-methyladenosine (m6A), which involves the addition of a methyl group to the sixth nitrogen of adenosine residues in RNA.m6A is the most prevalent internal modification found in eukaryotic messenger RNA (mRNA). It plays crucial roles in various cellular processes, including mRNA stability, splicing, translation, and degradation. The addition of m6A is regulated by a complex of proteins often referred to as "writers" (e.g., METTL3), while "erasers" (e.g., FTO and ALKBH5) remove these modifications. Additionally, "readers" (e.g., IGF2BP proteins) recognize m6A-modified mRNAs and mediate their regulatory effects. Recent research indicates that epitranscriptomic modifications, particularly m6A, are increasingly recognized for their role in kidney diseases, including chronic kidney disease (CKD). In CKD, there is accumulating evidence that heightened m6A modification can contribute to the pathology of kidney fibrosis and inflammation. Studies have shown that METTL3 expression and m6A modification levels are significantly elevated in diseased kidneys. This modification leads to stability in specific mRNAs associated with inflammatory responses, like those encoding key components of the cGAS-STING pathway (a vital player in immune signaling). The cGAS-STING pathway serves as a cytosolic DNA sensor that activates innate immune responses. In CKD, renal tubular cells often experience mitochondrial stress, causing the leakage of mitochondrial DNA into the cytosol. This leakage triggers the cGAS-STING pathway, resulting in inflammation and fibrosis. m6A modifications enhance the stability of cGAS and STING1 mRNAs, promoting an unwarranted inflammatory response.The research indicates that overexpression of METTL3 in renal tubular cells enhances inflammatory signaling. On the contrary, inhibiting METTL3 expression through tubule-specific gene deletion or antisense oligonucleotides