Unraveling the epitranscriptomic code: a breakthrough in early cancer detection

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Abstract

One of the greatest challenges in oncology is detecting cancer at its earliest stages—before it becomes an unstoppable force. While traditional biomarkers have fallen short, a new frontier is emerging: epitranscriptomics, the intricate chemical language of RNA modifications that orchestrates gene expression beyond the DNA sequence itself. More than 150 chemical marks have been identified across various RNA molecules, forming a dynamic and adaptive code that responds to environmental cues and fuels cellular evolution.

Our consortium has pioneered an analytical pipeline that fuses mass spectrometry with machine learning, enabling the large-scale profiling of RNA modifications from a minimal amount of sample. This innovative approach has uncovered distinct epitranscriptomic signatures that evolves with cancer progression, offering a powerful tool for diagnosis, prognosis, and treatment response prediction. Strikingly, certain RNA modifications are not just passive bystanders but active drivers of tumorigenesis, making them prime targets for cancer diagnostic & therapeutic intervention.

Unlike unmodified nucleosides, modified nucleosides cannot be recycled and are preferentially excreted, leaving telltale traces in blood and urine. Leveraging this phenomenon, we have successfully decoded an epitranscriptomic signature for colorectal cancer (CRC) by analyzing plasma samples from 47 patients and 20 healthy donors. A longitudinal study on an independent cohort (20 early-stage CRC patients—stages I and II—and 20 healthy donors samples) revealed a dynamic modulation of this signature following tumor resection, with expression levels gradually returning to values comparable to those observed in healthy donors. Recently, we validated the performance of this signature in an expanded independent cohort (131 CRC patients and 30 healthy donors), further reinforcing its potential for early cancer detection. Encouragingly, applying similar methodologies to other malignancies, including pancreatic and breast cancer, has yielded promising results.

This groundbreaking work positions multiplex RNA modification analysis as a game-changer in non-invasive cancer diagnostics, offering a revolutionary pathway to detect cancer before it takes hold. With its profound implications for precision medicine, this innovation has the potential to redefine cancer screening and treatment strategies—ushering in a new aera of personalized oncology.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

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