Analysis of Metabolic Dysfunction-Associated Non-coding Transcripts Involved in Hepatocellular Carcinoma Development.

Frida M. Delgadillo[1], Karla Perez[2], Shrikanth S. Gadad[2], Enrique Ramos[1]

1. Department of Biological Sciences, The University of Texas at El Paso, El Paso, TX
2. Department of Medicine and Oncology, The University of Texas Rio Grande Valley, McAllen, TX

Background: Chronic liver disease patients often develop Hepatocellular Carcinoma (HCC), a primary type of liver cancer and the third leading cause of cancer-related deaths. Metabolic dysfunction-associated steatotic liver disease (MASLD) is one such condition which, if left untreated, can advance to metabolic dysfunction-associated steatohepatitis (MASH) before leading to HCC. Transcriptomic analyses are crucial for the identification of genes affecting this development, as previous studies that have established the pathways involved in this progression have focused on protein-coding genes. Instead, we are expanding on our previous work (Delgadillo et al. 2026) by identifying novel non-coding transcripts which may serve as potential biomarkers or therapeutic targets that can prevent malignant transformation.

Methods: We reanalyzed data from three publicly available NCBI/GEO datasets that included Normal, MASLD, MASH and HCC samples. An end-to-end bulk RNA sequencing pipeline was utilized to harmonize and perform batch-correction for the reads to compare the counts between the different datasets.

Results: This analysis identified long noncoding RNAs (lncRNAs) that are differentially expressed among the MASLD, MASH, and HCC conditions. Additionally, lncRNAs showing a progressive directional change in their transcripts-per-million (TPM) from the metabolic conditions to HCC conditions were selected for future validation experiments.

Conclusion: This study broadens the scope of our previous work by expanding the identification of potential noncoding RNA-based MASLD/MASH and HCC biomarkers and therapeutic targets, which may aid in the prevention of HCC development.