JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

DOI: 10.14744/jilti.2025.02996
J Inonu Liver Transpl Inst 2025;3(3):89–95

Original Research

Transcriptomic Profiling of Paired Tumor and Non-Tumor Biopsies Identifies Dysregulated Genes in Hepatocellular Carcinoma

Zeynep Kucukakcali

Department of Biostatistics and Medical Informatics, Inonu University, Faculty of Medicine, Malatya, Türkiye

Abstract

Objectives: Hepatocellular carcinoma (HCC) is a highly heterogeneous malignancy with poor prognosis and limited biomarkers for early detection or targeted therapy. This study aimed to comprehensively analyze differential gene expression in paired tumor and adjacent non-tumor liver biopsies, in order to identify transcriptional alterations with potential diagnostic, prognostic, or therapeutic relevance.

Methods: We utilized the publicly available GSE64041 dataset, comprising 60 paired biopsies (120 samples in total) from HCC patients. Data preprocessing and normalization were conducted in R using the limma package. Differentially expressed genes (DEGs) were determined with thresholds of |log2 fold change| > 1 and adjusted p-value < 0.05. Visualization tools included box plots, density plots, Uniform Manifold Approximation and Projection (UMAP), volcano plots, and mean difference (MD) plots to ensure robust evaluation of expression patterns and biological clustering.

Results: The transcriptomic analysis revealed clear separation between tumor and non-tumor tissues. A total of 20 top-ranked DEGs were identified, including markedly upregulated genes such as REG3A, SPINK1, GPC3, SLC7A11, and AKR1B10, as well as downregulated genes including CRHBP, FCN3, OIT3, STAB2, and CLEC1B. Many of these genes are known to be involved in oncogenic signaling, ferroptosis regulation, immune evasion, and tumor suppression. UMAP clustering and DEG visualization confirmed distinct transcriptional landscapes, supporting the biological divergence of HCC tissues from normal liver.

Conclusion: This study highlights a panel of significantly dysregulated genes reflecting both oncogenic activation and tumor suppressor loss in HCC. The findings provide valuable insights into the molecular mechanisms of hepatocarcinogenesis and suggest potential biomarkers for diagnosis, prognosis, and therapeutic targeting. These results may contribute to improving early detection, guiding risk stratification, and supporting the development of precision medicine approaches in hepatocellular carcinoma.

Keywords: Biomarkers, Differentially expressed genes, Hepatocellular carcinoma, Paired biopsies, Transcriptomic profiling

Please cite this article as "Kucukakcali Z. Transcriptomic Profiling of Paired Tumor and Non-Tumor Biopsies Identifies Dysregulated Genes in Hepatocellular Carcinoma. J Inonu Liver Transpl Inst 2025;3(3):89–95".

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and accounts for approximately 75–85% of all liver cancers, representing a major cause of cancer-related mortality worldwide. According to the latest GLOBOCAN data, liver cancer is the sixth most frequently diagnosed cancer and the third leading cause

Address for correspondence: Zeynep Kucukakcali, MD. Department of Biostatistics and Medical Informatics, Inonu University, Faculty of Medicine, Malatya, Türkiye
E-mail: zeynep.tunc@inonu.edu.tr

Submitted Date: 26.09.2025 **Revised Date:** 21.11.2025 **Accepted Date:** 21.12.2025 **Available Online Date:** 14.01.2026
Journal of Inonu Liver Transplantation Institute - Available online at www.jilti.org

of cancer-related death, with more than 900,000 new cases and 830,000 deaths reported annually.[1] The incidence of HCC shows marked geographical variation, with the highest burden observed in East Asia and sub-Saharan Africa, largely reflecting the prevalence of chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. In Western countries, increasing rates of non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease are emerging as major risk factors.[2] Despite improvements in surveillance programs and therapeutic strategies, the prognosis of HCC remains poor, with a 5-year survival rate below 20% in most countries, primarily due to late-stage diagnosis, high recurrence rates, and limited treatment options.[3]

At the molecular level, HCC is recognized as a highly heterogeneous disease, both genetically and phenotypically. This heterogeneity arises from the interplay of genomic instability, somatic mutations, epigenetic modifications, and deregulated signaling pathways, including Wnt/β-catenin, MAPK, PI3K/AKT, and TGF-β.[3,4] Efforts to classify HCC into reproducible molecular subtypes have provided important insights into tumor biology. For example, expression-based classification studies have identified subgroups with distinct prognoses and associations with oncogenic signaling pathways.[5,6] However, these classification systems are still not integrated into routine clinical practice. One of the main limitations of existing studies is that they were primarily conducted on surgically resected tumor specimens, which are enriched for patients with preserved liver function and early-stage disease. This introduces a selection bias and does not adequately represent the molecular landscape of advanced HCC or cases associated with cirrhosis, which constitute the majority of the clinical population.

Gene expression profiling has emerged as a powerful approach for unraveling the molecular mechanisms of cancer and identifying potential biomarkers. Technologies such as microarrays and next-generation sequencing (RNA-seq) enable genome-wide evaluation of transcriptomic changes, providing valuable information on both protein-coding and non-coding RNAs.[7,8] In HCC, expression profiling has been applied to characterize dysregulated pathways, identify prognostic gene signatures, and explore therapeutic targets. For instance, several studies have demonstrated that transcriptomic signatures can predict patient survival, response to therapy, and risk of recurrence.[5,9] Despite these advances, the translation of gene expression signatures into clinical biomarkers remains limited due to variability in study design, patient cohorts, and analytical methods.

To address these gaps, the present study utilizes publicly available gene expression data from the GSE64041 dataset, which includes paired tumor and non-tumor liver biopsies from 60 patients with HCC. This study design provides several advantages: (i) paired sampling allows direct within-patient comparisons, reducing inter-individual variability; (ii) biopsy-derived material better represents real-world clinical scenarios, including patients with cirrhosis and various tumor stages; and (iii) integration of non-tumor liver tissue as a control enables the identification of truly tumor-specific alterations. Through differential expression analysis and visualization methods such as box plots, density plots, UMAP, volcano plots, and MD plots, we aimed to comprehensively characterize the transcriptional landscape of HCC.

By identifying the most significantly upregulated and downregulated genes, this study contributes to a deeper understanding of the molecular mechanisms underlying hepatocarcinogenesis. Moreover, the findings may highlight potential biomarkers for diagnosis, prognosis, or therapeutic targeting, supporting future translational applications and paving the way for integrative studies combining transcriptomic, genomic, and clinical data.

Methods

Dataset

The dataset used in this study was obtained from the NCBI Gene Expression Omnibus (GEO) under the accession number GSE64041. It consists of 60 paired liver biopsies collected from patients diagnosed with hepatocellular carcinoma (HCC), where each pair includes one sample from the tumor tissue and one from the adjacent non-tumor liver tissue. This design ensures direct within-patient comparisons, reducing variability caused by inter-individual differences and improving the reliability of identifying tumor-specific transcriptional changes.

The dataset provides a valuable resource for investigating the molecular features of HCC in a clinically relevant population. Since biopsies reflect the tumor microenvironment in situ, the expression profiles capture not only the intrinsic tumor cell signatures but also interactions with surrounding liver tissue. This makes the dataset particularly suitable for studying gene dysregulation patterns and for exploring potential biomarkers associated with disease progression and prognosis.

Gene Expression Analysis

Changes in the physiological or pathological state of an organism are reflected in corresponding alterations in gene expression patterns. Therefore, the systematic assessment of gene expression provides valuable insights into the underlying molecular mechanisms of health and disease. Among the available approaches, DNA microarray technology has become a widely adopted method for

transcriptome-wide analysis. This technique is based on the hybridization of complementary DNA (cDNA) derived from messenger RNA (mRNA) molecules to thousands of immobilized probes on a solid surface, each representing a specific gene sequence.[10] The resulting signal intensities allow for the simultaneous quantification of expression levels across the genome.

Such large-scale profiling enables the identification of differentially expressed genes between experimental or clinical groups, facilitating the discovery of molecular biomarkers, the characterization of disease subtypes, and the elucidation of signaling pathways involved in pathogenesis.[11] In biomedical research, microarray-based expression analysis has been successfully applied to clinical samples, including those from healthy individuals and patients with diverse disorders, providing a robust tool for both functional genomics and translational medicine.

Bioinformatics Analysis Phase

In this study, the gene expression profiles obtained from paired tumor and non-tumor liver biopsies of patients with hepatocellular carcinoma (HCC) were analyzed. Data preprocessing and normalization were carried out in R using the limma package, a widely used statistical framework for gene expression studies.[12] Limma applies linear modeling and empirical Bayes methods to improve variance estimation, making it particularly suitable for datasets with limited sample sizes. Differentially expressed genes (DEGs) were identified based on log2 fold change (log2FC) values and adjusted p-values. Genes with log2FC > 1 were classified as upregulated, while those with log2FC < –1 were considered downregulated.

To visualize the data, several complementary approaches were employed. Box plots were generated to assess the distribution and normalization of expression data across samples, ensuring comparability between tumor and non-tumor tissues. In addition, Uniform Manifold Approximation and Projection (UMAP) was applied to reduce dimensionality and provide an unsupervised overview of similarities and clustering patterns among the samples.

For the identification of significant DEGs, volcano plots were constructed, plotting log2FC against statistical significance (–log10 p-value). This visualization enables rapid recognition of the most strongly up- and downregulated genes, with red dots representing upregulated genes, blue dots representing downregulated genes, and black dots corresponding to non-significant changes. Alongside this, Mean Difference (MD) plots were used to illustrate the log2 fold change in relation to average expression values, offering an additional perspective on differential expression. The use of consistent color coding across these plots facilitated the interpretation of results and allowed clear differentiation between significantly dysregulated and non-significant genes.

Results

The study includes data from 60 hepatocellular carcinoma (HCC) patients, each contributing one tumor biopsy and one matched non-tumor liver biopsy, for a total of 120 tissue samples. To evaluate the distribution and normalization of the expression data, box plots were generated, as presented in Figure 1. These visualizations provided an overview of expression levels across all samples and confirmed that the data were properly normalized before further analysis. In the plots, tumor biopsies were labeled as cancer, while adjacent non-tumor tissues were labeled as normal, with color coding applied to distinguish the groups.

In addition, expression density plots were employed to further assess data quality. As shown in Figure 2, the density curves of cancer (green) and normal (purple) samples largely overlapped, demonstrating consistency in intensity distributions between groups. This overlap indicated that technical variation was minimized, ensuring that downstream differential expression analysis would reflect genuine biological differences.

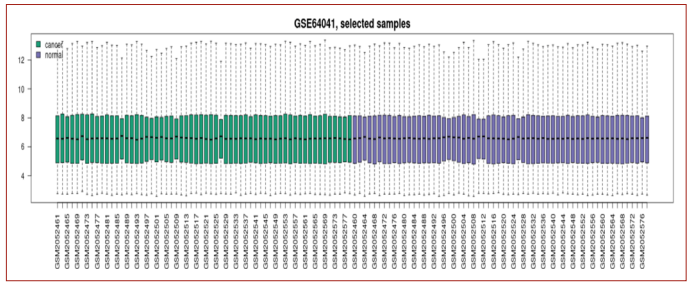

Figure 1. Box plot of gene expression values.

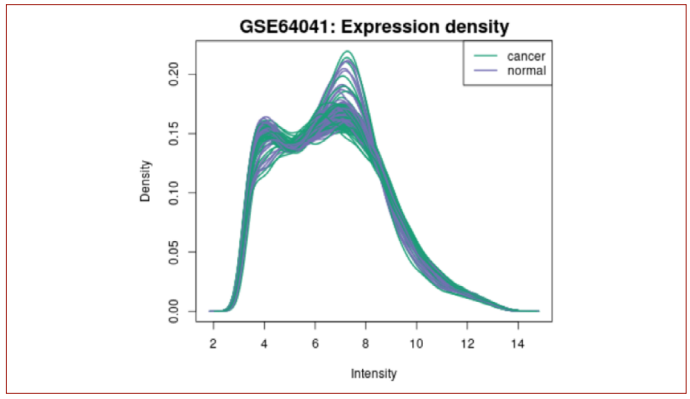

Figure 2. Expression density plot of samples (Density plot showing the distribution of expression intensities across cancer (green) and normal (purple) samples. The substantial overlap between the two groups confirms successful normalization and comparability of the datasets prior to differential expression analysis.).

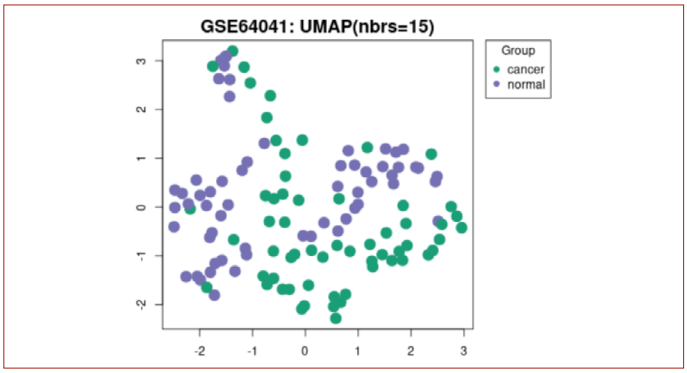

Figure 3. UMAP visualization of cancer and normal samples (UMAP plot based on expression data from 60 HCC patients (120 samples). Cancer (green) and normal (purple) tissues cluster separately, reflecting distinct transcriptional profiles.)

Figure 3 shows the UMAP plot generated from the expression profiles of the samples. This visualization demonstrates how samples with similar molecular characteristics cluster together in a reduced dimensional space. The distribution and clustering patterns provide important insights into the biological similarities and differences among the groups. In the graph, green dots represent cancer (tumor) tissue samples, while purple dots represent normal (non-tumor) liver tissue samples. The separation between these two groups highlights the distinct gene expression signatures of tumor and non-tumor tissues and illustrates the effectiveness of UMAP as a tool for visualizing heterogeneity and group classification within the dataset.

Based on the analysis of the GSE64041 dataset, the top 10 upregulated genes identified in the comparison between cancer (tumor) and normal (non-tumor) liver tissues are presented in Table 1. To ensure both statistical significance and biological relevance, threshold criteria were applied during differential expression analysis. Specifically, genes with an absolute log2 fold change (|log2FC|) greater than 1.0 and a p-value below 0.05 were considered significantly dysregulated.

These cut-off values provided a robust framework for distinguishing true biological differences from background noise. The upregulated genes identified under these conditions represent candidates of particular interest, as their consistent overexpression in cancer tissues may point to their involvement in tumor progression and carcinogenic pathways. Consequently, the results obtained from this analysis may offer valuable insights into potential biomarkers for diagnosis, prognosis, or therapeutic targeting in hepatocellular carcinoma.

Based on the analysis of the GSE64041 dataset, the top 10 downregulated genes identified in the comparison between cancer (tumor) and normal (non-tumor) liver tissues are presented in Table 2. For the identification of downregulated genes, the same statistical thresholds used for upregulation were applied. Specifically, genes with an absolute log2 fold change (|log2FC|) greater than 1.0 and a p-value below 0.05 were considered significantly downregulated.

These results highlight genes whose expression levels were consistently reduced in cancer tissues compared with normal liver tissues, suggesting potential roles as tumor suppressors or regulators of normal liver function that become impaired during hepatocarcinogenesis. The findings may provide further insight into molecular mechanisms underlying disease development and could support the identification of novel diagnostic or therapeutic biomarkers.

Figure 4 illustrates the volcano plot, which provides a comprehensive visualization of genes exhibiting differential expression between cancer (tumor) and normal (non-tumor) liver tissues. In this representation, the x-axis corresponds to the log2 fold change (log2FC), reflecting the magnitude and direction of expression changes, while the y-axis indicates statistical significance as –log10 (p-value). This dual-axis representation allows for the simultaneous evaluation of both the size and reliability of gene expression changes.

Table 1. Top 10 upregulated genes between cancer and normal tissue samples

ID	adj, P, Val	p	t	B	logFC	Gene symbol
8053341	4,18E-08	1,13E-09	6,603974	11,72321	2,624876	REG3A
8114964	1,41E-08	3,20E-10	6,856537	12,94729	2,350635	SPINK1
8084630	3,20E-12	1,48E-14	8,755112	22,65842	2,341945	NMRAL1P1
8175234	7,22E-09	1,42E-10	7,016854	13,73453	1,945761	GPC3
8102800	3,04E-11	2,16E-13	8,258221	20,04891	1,936128	SLC7A11
8167254	1,28E-07	4,10E-09	6,341416	10,47336	1,876775	SSX1
7927694	3,69E-11	2,71E-13	8,215627	19,82698	1,658532	PHYHIPL
8136336	2,05E-04	2,18E-05	4,418465	2,233265	1,61133	AKR1B10
7923086	5,02E-14	1,10E-16	9,651242	27,43665	1,5879	ASPM
8117054	7,79E-22	4,95E-26	13,56161	48,38471	1,574118	CAP2

Table 2. Top 10 downregulated genes between cancer and normal tissue samples

ID	adj, P, Val	p	t	B	logFC	Gene symbol
8106418	4,92E-19	1,48E-22	-12,0965	40,61003	-2,70026	CRHBP
7914075	6,18E-17	3,53E-20	-11,1056	35,27825	-2,61709	FCN3
7928330	2,82E-21	5,08E-25	-13,1323	46,12448	-2,52153	OIT3
8110183	5,99E-18	3,06E-21	-11,5475	37,6603	-2,42389	CDHR2
7958056	3,55E-22	1,07E-26	-13,8465	49,87529	-2,37671	STAB2
8148029	8,02E-16	7,76E-19	-10,5478	32,26708	-2,24046	COLEC10
7961102	1,47E-21	2,21E-25	-13,2856	46,93317	-2,23152	CLEC1B
7964183	5,60E-13	1,95E-15	-9,1272	24,63333	-2,21438	GLS2
8113369	2,54E-16	1,75E-19	-10,8162	33,71613	-2,19836	SLCO4C1
7968678	2,85E-16	2,40E-19	-10,7599	33,41227	-2,16527	FREM2

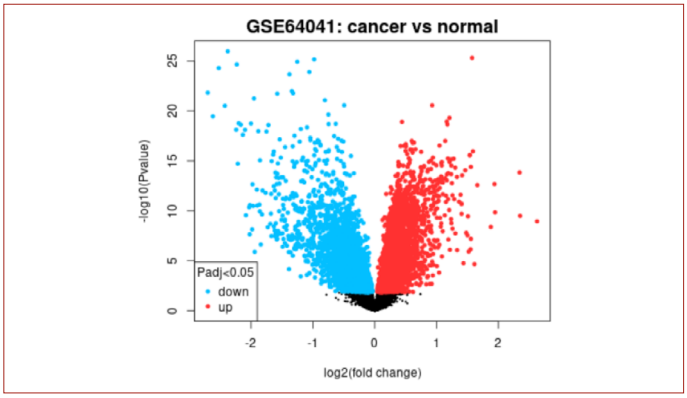

Figure 4. Volcano plot of differentially expressed genes between cancer and normal tissues.

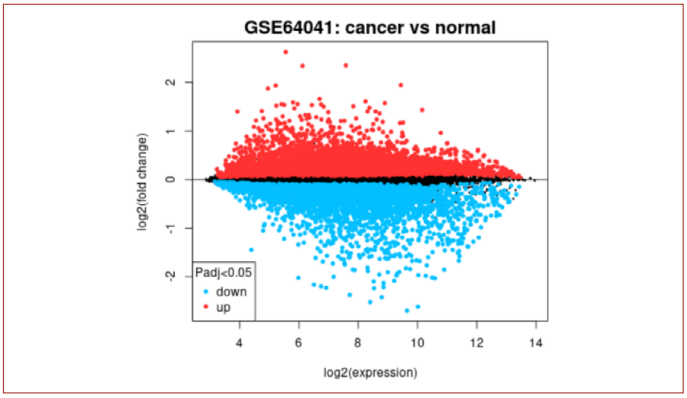

Figure 5. Mean Difference (MD) plot of gene expression between cancer and normal tissues.

In the plot, red dots represent significantly upregulated genes, while blue dots denote significantly downregulated genes. Genes that do not meet the established significance thresholds are shown in black, representing non-differentially expressed genes. The volcano plot therefore enables rapid identification of candidate biomarkers, as it highlights genes with both large fold changes and strong statistical support. This visualization is a widely used method in transcriptomic studies, as it effectively combines statistical significance with biological relevance, thereby providing an intuitive overview of the gene expression landscape within the dataset.

Figure 5 presents the Mean Difference (MD) plot, which provides a detailed visualization of the genes that display differential expression between cancer (tumor) and normal (non-tumor) liver tissues. In this plot, the x-axis corresponds to the average log2 expression level of each gene, while the y-axis represents the log2 fold change (log2FC), thereby combining both the baseline expression and the relative change in a single view. This dual representation makes the MD plot a powerful tool for detecting both subtle and pronounced alterations in gene expression.

Each point in the plot represents an individual gene. Red points indicate significantly upregulated genes, whereas blue points mark significantly downregulated genes, with color coding aiding in the rapid distinction of expression patterns. Genes that do not pass the significance threshold remain uncolored, providing a clear separation between relevant and background signals.

By visualizing expression levels in this way, the MD plot highlights not only global transcriptional trends but also emphasizes genes that deviate strongly from baseline expression, potentially serving as biomarker candidates. These dysregulated genes may be linked to critical pathways involved in hepatocarcinogenesis, offering valuable clues for understanding disease mechanisms and identifying possible therapeutic targets.

Discussion

In this study, we performed a comprehensive transcriptomic analysis of paired tumor and adjacent non-tumor liver biopsies from 60 hepatocellular carcinoma (HCC) patients using the GSE64041 dataset. This design, which incorporates matched samples from the same individuals, minimizes inter-patient variability and increases the robustness of the

findings by allowing direct comparison of tumor-specific transcriptional alterations against the background of the patient's own liver tissue. Differential expression analysis revealed distinct sets of upregulated and downregulated genes, highlighting not only known drivers of hepatocarcinogenesis but also novel candidates with potential diagnostic, prognostic, or therapeutic relevance. Importantly, the integration of multiple visualization strategies, including UMAP clustering, volcano plots, and mean difference plots, provided an intuitive overview of the transcriptional landscape and reinforced the biological separation between malignant and non-malignant tissues. Together, these results contribute to a more refined understanding of the molecular heterogeneity of HCC and may inform the development of precision medicine approaches aimed at improving early detection, risk stratification, and treatment outcomes in this highly lethal malignancy.

Among the most significantly upregulated genes, REG3A, SPINK1, GPC3, SLC7A11, and AKR1B10 emerged as key players. GPC3 has been widely validated as a diagnostic biomarker in HCC, with strong involvement in Wnt/β-catenin signaling and tumor proliferation.[13] SLC7A11, encoding the cystine/glutamate antiporter xCT, regulates glutathione synthesis and ferroptosis resistance, and its overexpression has been linked to poor prognosis and sorafenib resistance in HCC.[14] Similarly, AKR1B10 overexpression is consistently observed in HCC and has been associated with lipid metabolism, early carcinogenesis, and poor survival.[15,16] The upregulation of SPINK1 has also been implicated in promoting tumor growth and metastasis in HCC, potentially through EGFR pathway activation.[17] Collectively, the overexpression of these genes highlights their translational potential as biomarkers or therapeutic targets.

Conversely, several tumor suppressor candidates, including CRHBP, FCN3, OIT3, STAB2, and CLEC1B, were markedly downregulated. The reduced expression of STAB2, a scavenger receptor involved in hyaluronan clearance, has been linked to enhanced tumor progression and stromal remodeling.[18] CLEC1B, which contributes to platelet aggregation and immune regulation, has been reported as a prognostic marker, with lower levels associated with higher metastatic potential and poor outcomes in HCC.[19,20] Similarly, FCN3 and CRHBP downregulation may impair innate immune defense and stress response, thereby facilitating tumor development.[21,22]

The unsupervised UMAP clustering in this study clearly separated tumor and non-tumor tissues, underscoring the transcriptional divergence between groups. This observation aligns with prior large-scale transcriptomic classifications, such as those by Hoshida et al. and Boyault et al., which defined molecular subtypes of HCC with distinct signaling dependencies and clinical outcomes.[5,6] Importantly, the dysregulated genes identified in our dataset map onto pathways implicated in these molecular subclasses, reinforcing the robustness of our findings.

From a translational standpoint, the identified genes hold promise for both diagnostic and therapeutic applications. Serum-based detection of proteins such as GPC3 or AKR1B10 could facilitate earlier diagnosis, while expression status of SLC7A11 might guide ferroptosis-based therapies. Moreover, strategies aimed at restoring the expression of downregulated genes (e.g., CLEC1B or STAB2) may represent novel therapeutic directions.

Nevertheless, this study has limitations. First, it relied on a single dataset based on microarray technology, which does not capture the full spectrum of transcriptomic regulation, including non-coding RNAs and alternative splicing. Second, functional validation was beyond the scope of this analysis and is necessary to confirm the biological roles of the identified genes. Future studies integrating transcriptomic, genomic, and clinical data, along with experimental validation, will be crucial to translate these findings into clinical practice.

In summary, this transcriptomic analysis of paired biopsies highlights a panel of dysregulated genes that reflect both oncogenic activation and loss of tumor suppressor function in HCC. The results reinforce previously established molecular classifications while pointing to novel biomarker candidates that may improve diagnosis, prognosis, and therapeutic decision-making in hepatocellular carcinoma.

Disclosures

Ethics Committee Approval: Ethical approval was not required for this study, as all data were obtained from publicly available open-access datasets.

Funding: None.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: a cancer journal for clinicians 2021;71(3):209-49.
2. Villanueva A. Hepatocellular Carcinoma. The New England journal of medicine 2019;380(15):1450-62.
3. Llovet JM, Kelley RK, Villanueva A, et al. Hepatocellular carcinoma. Nature reviews Disease primers 2021;7(1):6.
4. Schulze K, Imbeaud S, Letouzé E, et al. Exome sequencing of hepatocellular carcinomas identifies new mutational signatures and

potential therapeutic targets. Nature genetics 2015;47(5):505-11.
5. Hoshida Y, Nijman SM, Kobayashi M, et al. Integrative transcriptome analysis reveals common molecular subclasses of human hepatocellular carcinoma. Cancer research 2009;69(18):7385-92.
6. Boyault S, Rickman DS, de Reyniès A, et al. Transcriptome classification of HCC is related to gene alterations and to new therapeutic targets. Hepatology (Baltimore, Md) 2007;45(1):42-52.
7. Wang Z, Gerstein M, Snyder M. RNA-Seq: a revolutionary tool for transcriptomics. Nature reviews Genetics 2009;10(1):57-63.
8. Golub TR, Slonim DK, Tamayo P, et al. Molecular classification of cancer: class discovery and class prediction by gene expression monitoring. Science (New York, NY) 1999;286(5439):531-7.
9. Chiang DY, Villanueva A, Hoshida Y, et al. Focal gains of VEGFA and molecular classification of hepatocellular carcinoma. Cancer research 2008;68(16):6779-88.
10. Schena M, Shalon D, Davis RW, et al. Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Science (New York, NY) 1995;270(5235):467-70.
11. Lockhart DJ, Winzeler EA. Genomics, gene expression and DNA arrays. Nature 2000;405(6788):827-36.
12. Ritchie ME, Phipson B, Wu D, et al. limma powers differential expression analyses for RNA-sequencing and microarray studies. Nucleic acids research 2015;43(7):e47.
13. Filmus J, Capurro M. Glypican-3: a marker and a therapeutic target in hepatocellular carcinoma. The FEBS journal 2013;280(10):2471-6.
14. Dai E, Han L, Liu J, et al. Autophagy-dependent ferroptosis drives tumor-associated macrophage polarization via release and uptake of oncogenic KRAS protein. Autophagy 2020;16(11):2069-83.
15. Liu R, Zheng S, yan Yang C, et al. Prognostic value of aldo-keto reductase family 1 member B10 (AKR1B10) in digestive system cancers: A meta-analysis. Medicine 2021;100(14):e25454.
16. DiStefano JK, Davis B. Diagnostic and prognostic potential of AKR1B10 in human hepatocellular carcinoma. Cancers 2019;11(4):486.
17. Yang C, Guo L, Du J, et al. Spink1 overexpression correlates with hepatocellular carcinoma treatment resistance revealed by single cell rna-sequencing and spatial transcriptomics. Biomolecules 2024;14(3):265.
18. Géraud C, Mogler C, Runge A, et al. Endothelial transdifferentiation in hepatocellular carcinoma: loss of Stabilin-2 expression in peri-tumourous liver correlates with increased survival. Liver international : official journal of the International Association for the Study of the Liver 2013;33(9):1428-40.
19. Jing Q, Yuan C, Zhou C, et al. Comprehensive analysis identifies CLEC1B as a potential prognostic biomarker in hepatocellular carcinoma. Cancer Cell International 2023;23(1):113.
20. Zhang G, Su L, Lv X, et al. A novel tumor doubling time-related immune gene signature for prognosis prediction in hepatocellular carcinoma. Cancer Cell International 2021;21(1):522.
21. Chen CC, Yu TH, Wu CC, et al. Loss of ficolin-3 expression is associated with poor prognosis in patients with hepatocellular carcinoma. International journal of medical sciences 2023;20(8):1091-96.
22. Xia HB, Wang HJ, Fu LQ, et al. Decreased CRHBP expression is predictive of poor prognosis in patients with hepatocellular carcinoma. Oncology letters 2018;16(3):3681-89.