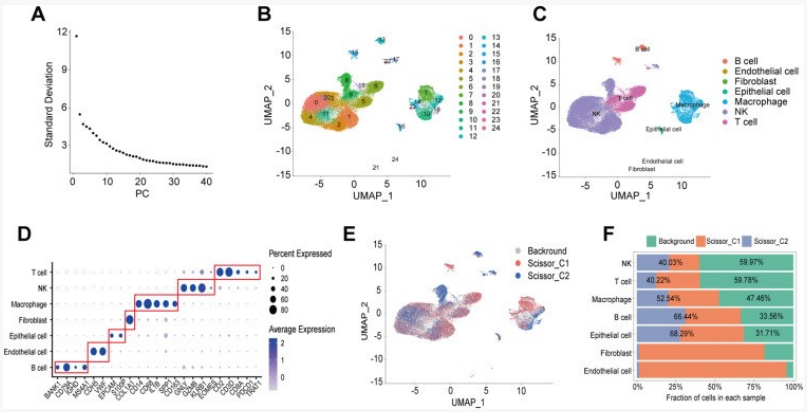
Immune Subtyping and NK Cell Targeting: Optimizing Immune Checkpoint Inhibitor Therapy in Hepatocellular Carcinoma

-New Study Unveils Novel Classification Approach for Predicting ICI Response in HCC Patients



(A) Number of principal components versus standard deviation under PCA analysis. (B) Visualization of cell clustering under the UMAP algorithm. (C) Distribution of annotated cells. (D) Average expression of marker genes on each cell. (E) Distribution of i

CHINA, March 18, 2025 /EINPresswire.com/ -- Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, accounts for about 75–85% of all liver cancer cases. Immune checkpoint inhibitors (ICIs), despite yielding a superior therapeutic impact, have substantial drawbacks, including therapy-resistant patients and absence of biomarkers for predicting the response to ICIs. Hence, there is an urgent need to investigate dependable biomarkers to enhance patient prognosis while minimizing the adverse effects of ICIs.

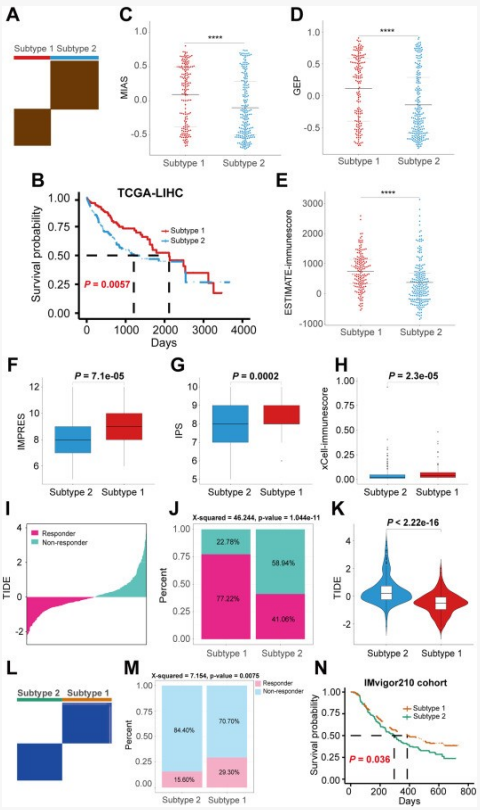
This research, published in the Genes & Diseases journal by a team from Chongqing Medical University, explores the heterogeneity of immune subtypes at the single-cell level using bulk and single-cell sequencing to identify potential ICI response-associated cells and therapeutic agents in HCC.

The researchers employed seven predictive scores related to ICI response to measure the effectiveness of an immune gene set in categorizing HCC patients. The results confirmed the ability of immune signature scores to distinguish two immune subtypes, subtype 1 and subtype 2, with significant differences in immune response. Patients in both subtypes showed varying overall survival, immunity levels, biological activities, and TP53 mutation rates. Furthermore, the study revealed that patients with subtype 1 demonstrated significantly improved overall survival rates and higher immune response scores compared to those with subtype 2.

Interestingly, this study noted that only subtype 1-associated natural killer (NK) cells showed a

positive correlation with immune-promoting scores, highlighting their potential role in enhancing ICI treatment efficacy. In addition, the researchers screened 2494 potential drugs using multiple databases and network approaches to identify potential therapeutic agents targeting subtype 1-associated NK cells. Among the candidates, docetaxel and thalidomide emerged as promising options for enhancing ICI response. Notably, sensitivity analysis revealed that docetaxel sensitivity in HCC patients rose as the levels of subtype 1-related NK cells increased, suggesting that increased sensitivity to docetaxel may enhance immune responses in HCC patients.

Although this research provides a framework for immune-based classification in HCC, the correlation between NK cell subsets and docetaxel sensitivity requires further validation through clinical trials. Nevertheless, the combination of subtype 1-associated NK cells and docetaxel may offer new hope for ICI treatment in HCC. In conclusion, this study has revealed the cell types that potentially affect ICIs and identified potential drugs by combining bulk sequencing and single-cell sequencing, which will provide a scientific reference for future studies of ICIs in HCC treatment.



(A) Unsupervised consistent clustering of the two subtypes of TCGA-HCC patients. (B) Comparison of overall survival (OS) between the two subtypes of TCGA-HCC patients. (C) Comparison of MIAS scores between the two subtypes of TCGA-HCC patients. (D) Compar

Reference

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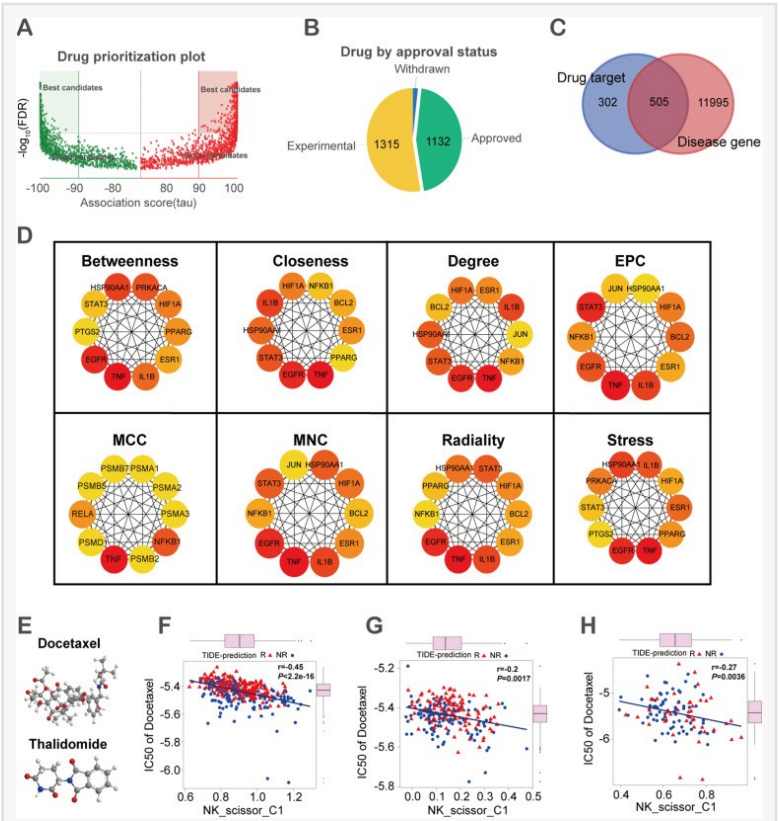

(A) Volcano plot of NK_scissor_C1-associated drug priorities. (B) NK_scissor_C1-associated drug usage status. (C) The Veen diagram showing intersections of NK_scissor_C1-associated drug targets with HCC-associated genes. (D) Interaction network of top 10

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