

## Combined Analysis of m<sup>6</sup>A and m<sup>5</sup>C Modulators on the Prognosis of Hepatocellular Carcinoma

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**Abstract :** Aim: Hepatocellular carcinoma (HCC) is one of the most common malignant tumors that endanger human health seriously. RNA methylation, especially N6-methyladenosine (m<sup>6</sup>A) and 5-methylcytosine (m<sup>5</sup>C), a crucial epigenetic transcriptional regulatory mechanism, plays an important role in tumorigenesis, progression and prognosis. This research aims to systematically evaluate the prognostic value of m<sup>6</sup>A and m<sup>5</sup>C modulators in HCC patients. Methods: Twenty-four modulators of m<sup>6</sup>A and m<sup>5</sup>C were candidates to analyze their expression level and their contribution to predict the prognosis of HCC. Consensus clustering analysis was applied to classify HCC patients. Cox and LASSO regression were used to construct the risk model. According to the risk score, HCC patients were divided into high-risk and low/medium-risk groups. The clinical pathology factors of HCC patients were analyzed by univariate and multivariate Cox regression analysis. Results: The HCC patients were classified into 2 clusters with significant differences in overall survival and clinical characteristics. Nine-gene risk model was constructed including METTL3, VIRMA, YTHDF1, YTHDF2, NOP2, NSUN4, NSUN5, DNMT3A and ALYREF. It was indicated that the risk score could serve as an independent prognostic factor for patients with HCC. Conclusion: This study constructed a Nine-gene risk model by modulators of m<sup>6</sup>A and m<sup>5</sup>C and investigated its effect on the clinical prognosis of HCC. This model may provide important consideration for the therapeutic strategy and prognosis evaluation analysis of patients with HCC.

**Keywords :** hepatocellular carcinoma, m<sup>6</sup>A, m<sup>5</sup>C, prognosis, RNA methylation

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