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LV BEST OP 3

Association between genetic features and serum biomarkers in hepatocellular carcinoma

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Introduction : Serum alpha-fetoprotein (AFP), Lens culinaris agglutinin−reactive AFP (AFP-L3), and des-gamma-carboxyprothrombin (DCP) are useful biomarkers of hepatocellular carcinoma (HCC). However, associations among molecular characteristics and serum biomarkers are unclear.

Methods : We analyzed RNA expression and DNA variant data from The Cancer Genome Atlas Liver Hepatocellular Carcinoma (TCGA-LIHC) to examine their associations with serum biomarker levels and clinical data. From 371 TCGA-LIHC patients, we selected 91 seen at 3 institutions in Korea and the United States and measured AFP, AFP-L3, and DCP from preoperatively obtained serum. We conducted an integrative clinical and molecular analysis, focusing on biomarkers, and validated the findings with the remaining 280 patients in the TCGA-LIHC cohort.

Results : Patients were categorized into 4 subgroups: elevated AFP or AFP-L3 alone (↑AFP&L3), elevated DCP alone (↑DCP), elevation of all 3 biomarkers (↑All), and reference range values for all biomarkers (RR). CTNNB1 variants were frequently observed in ↑DCP patients (n=7 [53.8%]) and RR patients (n=10 [38.5%]), but ↑DCP patients with a CTNNB1 variant had worse survival than RR patients. TP53 sequence variants were associated with ↑AFP (n=8 [30.8%]) and ↑DCP (n=4 [30.8%]). The Wnt− -catenin signaling pathway was activated in the ↑AFP&L3, whereas liver-related Wnt signaling was activated in the RR. TGF- and VEGF signaling are activated in high AFP&L3, while dysregulated bile acid and fatty acid metabolism were dominant in ↑DCP. We validated these finding using the remainder of the TCGA-LIHC cohort and showed similar results to the test cohort.

Conclusions : Serum AFP, AFP-L3, and DCP levels can help predict variants in the genetic profile

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