Epithelial-mesenchymal Transition Gene Signature to Predict Clinical Outcome of Hepatocellular Carcinoma

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Hepatocellular carcinoma is one of the most lethal cancers worldwide. More accurate stratification of patients at risk is necessary to improve its clinical management. As epithelial-mesenchymal transition is critical for invasiveness and metastasis of human cancers, we investigated expression profiles of twelve genes related to epithelial-mesenchymal transition through a real-time polymerase chain reaction. From a univariate Cox analysis for a training cohort of 128 hepatocellular carcinoma patients, four candidate genes (CDH1, ID2, MMP9, and TCF3) with significant prognostic values were selected to develop a risk score of patient survival. Patients with high risk scores calculated from the four-gene signature showed significantly shorter overall survival times. Moreover, the multivariate Cox analysis revealed that 4-gene signature (p=0.0026) and tumor stage (p=0.0023) were independent prognostic factors for overall survival. Subsequently, the 4-gene signature was validated in an independent cohort of 231 patients, in which high risk score was significantly correlated with shorter overall survival (p=0.0011) and disease-free survival (p=0.0001). When the risk score was entered in a multivariate Cox analysis with tumor stage only, both the risk score (p=0.0046) and tumor stage (p=2.6×10^{-5}) emerged as independent prognostic factors. In conclusion, we suggest that the proposed gene signature may improve the prediction accuracy for survival of hepatocellular carcinoma patients, and complement prognostic assessment based on important clinicopathologic parameters such as tumor stage.