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Z-score-based approach for differential diagnosis of malignant and benign liver neoplasms using transcriptional biomarkers

Mikhail S Chesnokov
N N Blokhin National Medical Research Center of Oncology, Russian Federation

Hepatocellular carcinoma (HCC) is the most common and aggressive type of liver tumors. It is usually diagnosed at advanced stages due to lack of clear symptoms and reliable biomarkers. HCC diagnosis is further complicated by high similarity between early HCC stages and benign liver neoplasms, especially hepatocellular adenoma. Efficient methods of HCC identification are required for establishing precise diagnosis and choosing optimal treatment strategy. Our group previously identified five genes (IQGAP3, RAB3B, GPC3, PRRX1 and CENPF) specifically overexpressed in HCC, but not in benign neoplasms or normal liver tissue. Present study evaluates the diagnostic efficiency of combinational indexes generated using expression levels of these genes and z-score approach. We examined paired samples of neoplastic and normal liver tissue collected from 50 HCC patients and 15 patients with hepatocellular adenoma or focal nodular hyperplasia. Gene expression levels were estimated using RT-qPCR, z-scores were calculated for single genes and all possible gene combinations. Z-score-based indexes were statistically processed using cohort comparison tests and ROC analysis to evaluate their usefulness for discerning HCC samples from normal liver tissue and benign neoplasms. IQGAP3, GPC3, PRRX1 and CENPF were significantly ($p<0.05$) overexpressed in HCC samples, but not in benign neoplasms, when compared to non-tumor liver tissue. RAB3B expression was increased in benign cohort and further elevated in HCC cohort. The most efficient combinations for HCC tissue identification were RAB3B+IQGAP3+PRRX1 (if both neoplastic and non-tumor tissue samples were used, ROC AUC=0.973) and RAB3B+PRRX1+CENPF (if only neoplastic samples were processed, ROC AUC=0.961). Both combinations displayed sensitivity and specificity levels higher than 90%. In summary, RAB3B, IQGAP3, PRRX1 and CENPF are promising biomarkers for improving HCC diagnosis efficacy. Z-score calculation is a powerful tool for combining expression levels of multiple genes into one index that can be used as an efficient biomarker. Present study was funded by RFBR according to the research project № 18-315-00376.

Biography

Mikhail S Chesnokov has completed his PhD from N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russian Federation. He worked as a research associate in Lab of Epithelial Tumor Progression Mechanisms, Institute of Carcinogenesis, studying molecular mechanisms of pancreatic and liver cancer progression. Over last several years he published a number of research papers and participated in numerous international conferences reporting novel regulators of pancreatic ductal adenocarcinoma development and putative biomarkers of hepatocellular carcinoma. He recently moved to The Hormel Institute, University of Minnesota, USA, to apply his experience and skills in the field of targeted anti-cancer therapy focused on eradication of stem-like cancer cells in ovarian tumors via necroptotic cell death induction. Mikhail's major areas of interest in regard to cancer research are regulatory mechanisms of malignant cell differentiation, diagnostic biomarkers for early cancer diagnosis and search for novel molecular targets that can be used for efficient anti-tumor therapy.

m.chesnokov.oncology@gmail.com

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