

Hepatic diseases related peripheral blood RNAs variation and their clinical significance

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Background: Hepatocellular carcinoma (HCC) is a very complicated cancer and one of the leading causes of cancer death worldwide. However, mechanisms underlying the genesis and progression of the disease are far from clear and it has no high sensitive and high specificity biomarker to diagnosis the disease. MicroRNAs (miRNAs) in serum and blood Genome-wide gene expression profiling of clinical samples may represent an effective approach to gain relevant information. They might be emerging as promising biomarkers for several pathological conditions. Our aim was to investigate the feasibility of using circulating miRNAs and mRNA profiling as biomarker for liver pathologies.

Methods and Results: After histological identification, a total of 9 small Hepatocellular carcinoma peripheral blood samples and 5 health control peripheral blood samples were profiled using Affymetrix microarray platform. Data analysis was performed by Benjamini&Hochberg correction of two-sample T Test unpaired with genespring 10.0 analysis software. We found 726 probe sets were significantly differential regulated ($P < 0.05$, fold change > 2.00). Of these, 103 probe sets were up-regulated and 623 probe sets were down-regulated. In these differentially regulated genes, CXCR4, IL8, PFDN5, CALR and GOS2 were validated highly correlated with GeneChip results by the GenomeLab GeXP Genetic Analysis System.

Real-time quantitative PCR-based TaqMan MicroRNA Arrays were initially employed to profile miRNAs in serum pools from patients with hepatocellular carcinoma (HCC), liver cirrhosis (LC) and healthy control, respectively. Five miRNAs (i.e., miR-885-5p, 574-3p, -224, -215 and -146a) with potentially up-expressed levels in both HCC and LC serum pools were selected and further quantified in patients with HCC, LC, chronic hepatitis B (CHB), gastric cancer (GC) and normal controls using RT-qPCR. More than 110 miRNAs species in serum samples were detectable and great distribution ranges of serum miRNAs have been observed. Significant increase of miR-885-5p in sera of patients with HCC, LC, and CHB were found when compared to healthy control and GC. More importantly, miR-885-5p yielded an AUC (the area under the ROC curve) of 0.904 (95% CI: 0.837-0.951; $p < 0.0001$) with 90.53% sensitivity and 79.17% specificity in discriminating liver pathologies from healthy control, using the cut-off value of 1.06 (normalized). No evident correlations between increased miR-885-5p and liver function parameters (AFP, ALT, AST and GGT) in patients with liver pathologies were observed.

Conclusion: The molecular signatures were clearly different between small HCC and health control. It was also indicated that the five genes: CXCR4, IL8, PFDN5, CALR and GOS2 could be sensitive markers for the differential diagnosis of health control, small HCC and other liver disease including virus hepatitis and liver cirrhosis. We also concluded that miR-885-5p is significantly elevated in serum of patients with liver pathologies and our data suggest that serum miRNAs may deserve to be explored to serve as novel complimentary biomarkers for the detection and assessment of liver pathologies.

Biography

Yaping Tian received his Master Degree in Medicine from Chinese PLA Postgraduate Medical School and PhD from Academy of Military Medical Sciences. He had been trained as Postdoctoral Fellow for 2 years in The Queen Elizabeth Hospital, Australia. His researching interesting focused on the specific serum proteomic profiles and genetic signatures in different diseases, especially on cancer. He also interested in the studies of antioxidants in herbal medicine and free radical biology. More than 300 Chinese or English writing scientific papers in peer-reviewed journals have been published. He is on the editorial boards of several journals and the chairman of the Clinical Biochemistry and Applied Molecular Biology Association, CSBMB.

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