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Integrated analysis of gene expression profiles reveals deregulation of the immune response genes during different phases of chronic hepatitis B infection

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Abstract

© 2017, Kowsar Corp. Background: The natural history of chronic hepatitis B (CHB) infection is divided into different phases including immune tolerance (IT), immune clearance (or immune active [IA]), inactive carrier (IC), and reactivation. Despite utilizing high-throughput data, the distinct immunological mechanisms of these phases have been insufficiently investigated. Objectives: The aim of the present study was to determine candidate disease-associated genes and significantly altered biological processes for each phase of CHB infection. Methods: The gene expression profiles of 83 CHB patients (22 IT, 50 IA, and 11 IC phases) were obtained from gene expression omnibus (GEO dataset: GSE65359) and analyzed by bioinformatics tools. Several plugins of Cytoscape software were used to construct protein-protein interaction (PPI) networks and measure their topological properties. Subsequently, functional annotation and signaling pathway enrichment were carried out using the database for annotation, visualization and integrated discovery (DAVID) and Kyoto encyclopedia of genes and genomes (KEGG). Results: 449 and 452 deregulated genes were identified in IT-IA and IA-IC patients, respectively. Gene ontology and KEGG pathway analyses showed that several immune response-associated genes and signaling pathways (i.e. cytokine-cytokine receptor interaction, chemokine signaling pathway and T cell receptor signalling pathway) were upregulated in the IA phase, but downregulated in the IC phase. The LCK (encoding a tyrosine kinase) was determined as the most important hub gene of both constructed PPI networks. Furthermore, other immune response-associated genes such as CXCR3, VCAN, MYC, and STAT1 were found to be the important hub genes in clinical phases of CHB. Conclusions: The immune response-related pathways were found to be up and downregulated in the immune clearance phase and inactive carrier phase of CHB, respectively. The LCK hub gene might help the pathogenesis of different phases of CHB and serve as a therapeutic target for the treatment of hepatitis B virus.

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Keywords

Chronic Hepatitis B, Gene Ontology, Immune Clearance, Immune Tolerant, Inactive Carrier

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