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Original Article

Comparison of the inhibitory and stimulatory effects of Core and NS3 candidate HCV vaccines on the cellular immune response

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Abstract: Currently, hepatitis C virus (HCV) infects nearly 3% of the global population, the majority of whom are chronically infected; however, hepatitis C vaccines are still in the developmental stage. Numerous studies suggest that the spontaneous resolution of HCV infection and the design of its vaccine are reliant on vital contributions from CTL cell responses and T regulatory cells. Multiple researchers have identified both Core and nonstructural protein 3 (NS3) proteins as crucial immune genes and potential candidates for HCV DNA vaccine design. In this study, Core and NS3 were subcloned and inserted into pcDNA3.1 to construct HCV DNA vaccines administered in mouse models. Furthermore, the effects of Core and NS3 on the induction of CTL and NK were compared in spleen mouse models using the LDH method. Additionally, flow cytometry was employed to investigate the percentage of T regulatory cells (Treg cells) and cells expressing PD-1 in the spleens of the mouse models. Our data indicated that pcDNA3.1+NS3 and pcDNA3.1+Core could enhance CTL and NK activity in mouse models. Importantly, the Treg and PD-1 analysis in mouse models revealed a substantial reduction in the proportions of CD4+/CD25+/Foxp3+ T cells and PD-1+ cells in experimental subjects treated with HCV NS3 along with 5 mg/kg of lenalidomide, utilized as a novel adjuvant, compared to those administered an equivalent dosage of lenalidomide in conjunction with HCV Core. In conclusion, our observations indicated that the NS3-HCV gene had a limited impact on the activation of inhibitory factors. Therefore, NS3 is considered a more suitable candidate for DNA vaccine design compared to Core HCV.

Keywords: HCV, Core, NS3, vaccine, CTL cell, T regulatory cells

Introduction

HCV is among the main factors in acute and chronic liver diseases such as hepatocellular carcinoma and cirrhosis [1-3]. According to studies conducted by the WHO, 170 million people currently suffer from HCV, and 3 to 4 million, mostly in developing countries, are newly affected by this disease each year globally. Despite significant efforts in producing an HCV vaccine, the development of such a vaccine has encountered several obstacles, namely a lack of animal models, genetic heterogeneity, and several effective immune escape strategies. Although neutralizing antibodies against HCV can be identified within 7-8 weeks post-infection, they cannot successfully protect the infected person against reinfection. However, cellular immunity is capable of clearing HCV infection, implying its importance in spontaneous resolution of acute HCV and long-term protection from persistent infection [4-6]. Furthermore, regulatory T cells have a pathologic role in viral infection, especially in chronic infections and vaccine design in humans. It has been shown that the number of circulating CD4+/CD25+/Foxp3 cells in HCV carriers is larger than that of healthy persons. Treg cells also inhibit CTL cells and IFN-γ secretion, which results in delayed virus clearance and persistent infection. In most cases, CD8 cytotoxic T-lymphoid (CTL) responses were associated with the control of infectious agents, especially against viral infection or tumor Ag-derived pep-

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Disclosure of conflict of interest

None.

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