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Commentary

Immune Tolerance for Viral Hepatitis Diseases and Hepatocellular Carcinoma

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DESCRIPTION

Liver diseases are a major cause of morbidity and mortality worldwide, affecting millions of people. Some of the common liver diseases include viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease, autoimmune hepatitis, and liver cancer. These diseases can lead to chronic inflammation, fibrosis, cirrhosis, and Hepatocellular Carcinoma (HCC), the most common type of primary liver cancer. Immunotherapy is a potential strategy to treat liver diseases by harnessing the power of the immune system to fight against pathogens, tumor cells, or fibrotic cells. Vaccination is one of the immunotherapy approaches that aim to elicit specific immune responses against a target antigen by introducing a vaccine that contains the antigen or its fragments. Vaccination can be used to prevent or treat infections, cancers, or autoimmune diseases by stimulating protective immunity or modulating immune tolerance.

Some of the vaccination-based immunotherapies have been developed or are under investigation for liver diseases. Viral hepatitis is a major cause of liver disease and HCC worldwide. Hepatitis A Virus (HAV) and Hepatitis B Virus (HBV) are preventable by effective vaccines that induce long-lasting immunity. Hepatitis C Virus (HCV) has no vaccine available yet, but can be cured by antiviral drugs. However, there are still millions of people who are chronically infected with HBV or HCV and are at risk of developing liver complications. Vaccination for HBV can prevent new infections and reduce the transmission of the virus. However, it cannot eliminate the virus from those who are already infected and have established chronic infection. Therefore, therapeutic vaccination is needed to boost the immune response against HBV and achieve viral clearance or functional cure. Several therapeutic vaccines have been tested in clinical trials for chronic hepatitis B, but none has shown satisfactory efficacy so far. One of the challenges is to overcome the immune tolerance induced by the liver microenvironment and the persistent antigen exposure. One capabile strategy is to combine vaccination with immune-modulators that can enhance the vaccine-induced immunity and break the immune tolerance. For example, a recent study showed that an IL-12-based vaccination therapy could reverse liver-induced systemic tolerance toward HBV by restoring systemic HBV-specific CD4+ T cell responses, eliciting robust hepatic HBV-specific CD8+ T cell responses, and facilitating the generation of HBs Ag-specific humoral immunity in a mouse model. This therapy may become a viable approach to treat patients with chronic hepatitis B in the future.

Liver cancer is one of the most lethal cancers worldwide, with HCC being the predominant type. The main risk factors for HCC include chronic viral hepatitis, alcohol consumption, metabolic syndrome, and aflatoxin exposure. The current treatments for HCC include surgery, transplantation, ablation, embolization, chemotherapy, and targeted therapy. However, these treatments have limited efficacy and are associated with high recurrence rates and adverse effects. Immunotherapy has emerged as a new paradigm for cancer treatment by activating the anti-tumor immune response or inhibiting the immunosuppressive mechanisms. Vaccination is one of the immunotherapy modalities that aim to induce tumor-specific immune responses by presenting tumor antigens to the immune system. Several types of vaccines have been developed for HCC, such as peptide vaccines, dendritic cell vaccines, viral vector vaccines, DNA vaccines, and RNA vaccines.

CONCLUSION

Vaccination-based immunotherapy is a potential strategy to prevent or treat various liver diseases by stimulating specific immune responses against pathogens, tumor cells, or fibrotic cells. Several vaccines have been developed or are under investigation for viral hepatitis, liver cancer or fibrosis using different antigens and delivery systems. However, there are also some challenges and limitations such as antigen selection, immune tolerance, immunosuppression, and safety issues that need to be addressed before vaccination therapy can be widely applied in clinical practice. These vaccines can target Tumor-Associated Antigens (TAAs) or neoantigens that are derived from tumor mutations.

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