Feasibility of immunotherapy in HCC

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Viral hepatitis B is an enigmatic disease in which the host's own immune response to persistent viral infection may bring about host destruction through antiviral inflammatory responses. Although the immunoprophylactic vaccine against hepatitis B, which is able to prevent viral infection, has been licensed in 1981, chronic hepatitis and hepatocellular carcinoma (HCC) induced by HBV or HCV are still being issued. One of current approaches, which are purposed to develop therapeutics against hepatitis, is an immunotherapy. Its distinct peculiarity is to utilize host immune systems capable of recognizing / discriminating the infected cells as non-self. Whether or not this approach is able to be developed into successful therapeutics seems to be dependent on multiple factors including antigenicity and delivery tools like that. So far, several promising approaches such as immunotherapy including epitope-based therapeutic vaccines, cell therapy including dendritic therapy, DNA vaccine including viral vectors, and gene silencing technology by RNA interference, have been proposed and evaluated. We also examined the feasibility whether adoptive immunotherapy by using antigen-specific cytotoxic T lymphocyte (CTL) is available for the HCC therapy. To this end, human CTLs recognizing specific epitopes derived from HBx antigen were cloned from HBV-infected patients. What we found was that, in xenografted nude model, those cells showed potential effect in eradication of xenografted human hepatoma. In the meantime, we also found several tricky-points such as antigenic mimicry, degeneracy effects, limited applications and etc. in doing the development of single epitope-based approach. These are critical battle rackets to develop therapeutics by using immune cells just like CTL. To overcome these problems, we recently develop 'supertype epitopes-based approach'. In this approach, we tried to find more universal and general epitopes, which are able to apply for immunotherapy targeted to hepatitis. Through general binding properties, we built theoretical background up for screening supertype epitopes, and selected novel supertype epitopes derived from HCV viral antigens. In ex vivo study by using PBMCs derived from hepatitis patients (chronic, acute, liver cirrhosis and HCC), interestingly, we found that a significant number of
CTLs capable of recognizing supertype epitopes are existed in most of all patients. This result suggests that these supertype epitopes may potentially be available for the immunological therapeutics against viral hepatitis. Furthermore, the concept of supertype epitope may be applied to the development of therapeutics against other viral diseases as well as cancers.
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