Development of Th1 and Th2 populations and the nature of immune responses to hepatitis B virus DNA vaccines can be modulated by codelivery of various cytokine genes

李岳倫

Chow YH;Chiang BL;Lee YL;Chi WK;Lin WC;Chen YT;Tao MH

摘要

Abstract

In this study, we provide direct evidence that the magnitude and nature of the immune response to a DNA vaccine can be differentially regulated by codelivery of various mouse cytokine genes. Mice immunized with a hepatitis B virus (HBV) DNA vaccine and the IL-12 or IFN-gamma gene exhibited a significant enhancement of Th1 cells and increased production of anti-HBV surface IgG2a Ab, as well as a marked inhibition of Th2 cells and decreased production of IgG1 Ab. In contrast, coinjection of the IL-4 gene significantly enhanced the development of specific Th2 cells and increased production of IgG1 Ab, whereas Th1 differentiation and IgG2a production were suppressed. Coinjection of the IL-2 or the granulocyte-macrophage-CSF gene enhanced the development of Th1 cells, while the development of Th2 cells was not affected, and the production of IgG1 and IgG2a Ab were both increased. The CTL activity induced by HBV DNA vaccination was most significantly enhanced by codelivery of the IL-12 or IFN-gamma gene, followed by the IL-2 or granulocyte-macrophage-CSF gene, whereas codelivery of the IL-4 gene suppressed the activity. When challenged with HBV surface Ag (HBsAg)-expressing syngeneic tumors, significant reduction of tumor growth was observed in mice that were coadministered the IL-12 gene but not the IL-4 gene. Taken together, these results demonstrate that application of a cytokine gene in a DNA vaccine formulation can influence the differentiation of Th cells as well as the nature of an immune response and may thus provide a strategy to improve its prophylactic and therapeutic efficacy.