A novel therapeutic hepatitis B vaccine induces cellular and humoral immune responses and breaks tolerance in hepatitis B virus (HBV) transgenic mice.

Abstract: Therapeutic vaccines are currently being developed for chronic hepatitis B and C. As an alternative to long-term antiviral treatment or to support only partially effective therapy, they should activate the patient's immune system effectively to fight and finally control the virus. A paradigm of therapeutic vaccination is the potent induction of T-cell responses against key viral antigens - besides activation of a humoral immune response. We have evaluated the potential of a novel vaccine formulation comprising particulate hepatitis B surface (HBsAg) and core antigen (HBcAg), and the saponin-based ISCOMATRIX(TM) adjuvant for its ability to stimulate T and B cell responses in C57BL/6 mice and its ability to break tolerance in syngeneic HBV transgenic (HBVtg) mice. In C57BL/6 mice, the vaccine induced multifunctional HBsAg- and HBcAg-specific CD8+ T cells detected by staining for IFN?, TNF?, and IL-2, as well as high antibody titers against both antigens. Vaccination of HBVtg animals induced potent HBsAg- and HBcAg-specific CD8+ T-cell responses in spleens and HBcAg-specific CD8+ T-cell responses in livers as well as anti-HBs seroconversion two weeks post injection. Vaccination further reduced HBcAg expression in livers of HBVtg mice without causing liver damage. In
summary, this study demonstrates therapeutic efficacy of a novel vaccine formulation in a mouse model of immunotolerant, chronic HBV infection.