Immunostimulatory RNA is a potent inducer of antigen-specific cytotoxic and humoral immune response in vivo.

Abstract:
Single-stranded RNA stimulates immune cells and induces the secretion of pro-inflammatory cytokines and type I IFN. As adjuvant RNA can induce a Th2 type of humoral response, however, its potency in the induction of cytotoxic T cells in vivo has not been analyzed. Here we show that immunization with the antigen ovalbumin (OVA) and the adjuvant phosphodiester RNA complexed to the cationic lipid N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium methylsulfate (DOTAP) induced a Toll-like receptor-7-dependent cytotoxic T cell and humoral response. Staining with SIINFEKL-K(b) tetramers demonstrated the induction of antigen-specific T cells that were functional in in vivo cytotoxic T cell assays against SIINFEKL-loaded target cells. In infection experiments with OVA-secreting Listeria monocytogenes, the cytotoxic T cell response strongly reduced the bacterial load in liver and spleen. The RNA-driven humoral response was characterized by OVA-specific antibodies of the IgG1 isotype whereas CpG-DNA induced antigen-specific antibodies of the IgG2a (BALB/c) or IgG2c (C57BL/6) isotype. Furthermore, stimulation with RNA did not induce splenomegaly, a common feature of CpG-DNA-driven immune activation in mice. Taken together, our data confirm that RNA can be used as a safe adjuvant and
induces a strong antibody response of the IgG1 isotype. Additionally, we demonstrate that RNA induces an antigen-specific immunity characterized by a potent cytotoxic T cell response to infection.