Antigen delivery to CD11c+CD8- dendritic cells induces protective immune responses against experimental melanoma in mice in vivo.

Abstract:
Dendritic cells (DCs) are central modulators of immune responses and, therefore, interesting target cells for the induction of antitumor immune responses. Ag delivery to select DC subpopulations via targeting Abs to DC inhibitory receptor 2 (DCIR2, clone 33D1) or to DEC205 was shown to direct Ags specifically to CD11c(+)CD8(-) or CD11c(+)CD8(+) DCs, respectively, in vivo. In contrast to the increasing knowledge about the induction of immune responses by efficiently cross-presenting CD11c(+)CD8(+) DCs, little is known about the functional role of Ag-presenting CD11c(+)CD8(-) DCs with regard to the initiation of protective immune responses. In this study, we demonstrate that Ag targeting to the CD11c(+)CD8(-) DC subpopulation in the presence of stimulating anti-CD40 Ab and TLR3 ligand polyinosinic-polycytidylic acid induces protective responses against rapidly growing tumor cells in naive animals under preventive and therapeutic treatment regimens in vivo. Of note, this immunization protocol induced a mixed Th1/Th2-driven immune response, irrespective of which DC subpopulation initially presented the Ag. Our results provide important...
information about the role of CD11c(+)CD8(-) DCs, which have been considered to be less efficient at cross-presenting Ags, in the induction of protective antitumor immune responses.