Journal for ImmunoTherapy of Cancer

POSTER PRESENTATION Open Access

Epitope optimization of a DNA vaccine targeting SSX-2 leads to PD-1 upregulation on antigen-specific CD8 T cells and PD-L1 upregulation on tumor cells

Brian Rekoske*, Heath A Smith, Douglas G McNeel

From Society for Immunotherapy of Cancer 28th Annual Meeting
National Harbor, MD, USA. 8-10 November 2013

Background

Recent groups have shown that the immunological efficacy of vaccines could be increased by encoding targeted mutations that enhance the binding affinity between the encoded epitopes and the MHC-TCR complex. In this study, we sought to examine the anti-tumor efficacy of a DNA vaccine targeting SSX-2, a cancer-testis antigen (CTA) expressed by prostate tumors, containing mutations designed to enhance the affinity of the reactive epitopes for the MHC.

Methods

A mouse sarcoma line engineered to express human HLA-A2 and SSX-2 was subcutaneously implanted into the hind flanks of C57BL/6 mice engineered to express HLA-A2 and not express mouse MHC types (HHDII-DRI mice). Mice were then treated with either a control DNA vaccine, a plasmid encoding the native SSX-2, or a plasmid encoding SSX-2 with optimized HLA-A2-binding epitopes, and tumor growth was followed.

Results

Immunization of mice with plasmid encoding native or epitope-optimized SSX-2 elicited SSX-2 specific HLA-A2-restricted CD8+ T cells as measured by IFNγ ELISpot that were able to lyse SSX-2-expressing target cells. Despite a greater frequency of SSX-2-specific CD8+ T cells detectable following immunization with the optimized vector, immunization with the optimized vector had an inferior anti-tumor response in vivo compared with the native SSX-2 vaccine. The SSX-2-specific CD8+ T cells elicited from the optimized vaccine expressed higher levels of programmed death-1 (PD-1) compared to those elicited from the native SSX-2- vaccine, and its ligand PD-L1 was shown to be induced on the surface of tumors following immunization and could be induced in vitro by co-culturing with splenocytes from immunized animals. Ongoing studies are evaluating the efficacy of immunization with concurrent blockade of the PD-1 axis.

Conclusions

Although much work has been directed at developing optimized cancer vaccines, our work suggests that the PD-1/PD-L1 axis serves as a dominant compensatory mechanism of resistance to this approach. Optimal next-generation DNA vaccines will likely need to be designed in such a way to either avoid or block the PD-1 regulatory pathway in order to increase their anti-tumor efficacy.

Published: 7 November 2013

doi:10.1186/2051-1426-1-S1-P233
Cite this article as: Rekoske *et al.*: Epitope optimization of a DNA vaccine targeting SSX-2 leads to PD-1 upregulation on antigen-specific CD8 T cells and PD-L1 upregulation on tumor cells. *Journal for ImmunoTherapy of Cancer* 2013 **1**(Suppl 1):P233.

Department of Medicine, University of Wisconsin-Madison, Madison, WI, USA