OPTIMIZING IMMUNIZATION SCHEDULES FOR THERAPEUTIC VACCINATION

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Background Most cancer vaccines will not generate high levels of T-cell immunity with only one immunization. Even vaccines against foreign antigens, such as COVID, may require three or four immunizations spaced some months apart to achieve protective levels of immunity in cancer patients. The use of cancer vaccines in the therapeutic setting, as single agents or as part of a combination regimen to treat established cancers, would require high levels of T-cells to be generated quickly. We evaluated immunization schedules with a 5-antigen, multiepitope plasmid DNA vaccine, STEMVAC, targeting cancer stem cell associated proteins. The vaccine is immunogenic in patients with advanced breast cancer (NCT02157051) and the majority of patients can develop high levels of STEMVAC specific type I T-cells after 3 priming and 2 booster immunizations. Using a murine model, we questioned whether we could more rapidly achieve high levels of antigen specific Type I T-cells with STEMVAC immunization.

Methods Six-week-old FVB mice were used for experiments. A dose of 300ug of STEMVAC plasmid with 5ug of rm-GM-CSF as an adjuvant was given in 4 immunizations using three different schedules; (1) every 3-4 days, (2) once a week, and (3) every 2 weeks (standard). Immunogenicity was evaluated two weeks after the last vaccine using IFN-gamma ELISPOT quantitating responses to each of the 5 antigens in the vaccine. Parameters studied included magnitude, incidence, and breadth of the T-cell response. Ten mice were included/group with empty plasmid and PBS as controls.

Results All three immunization schedules could generate a significant IFN-gamma response to at least one of the antigens encoded in STEMVAC as compared to controls. Vaccines given every two weeks elicited the greatest magnitude immune response among the three schedules (vs. 3-4 days, p=0.001; vs. 1 week, p=0.01). Of note, although the total magnitude of immune response elicited was lower, the weekly immunization schedule resulted in a significantly greater number of mice responding to vaccination as well as a greater breadth of response with all mice responding to at least 2 antigens and 50% to 3-5 antigens.

Conclusions Varying the time between immunizations can significantly impact the quality of the T-cell response to a multiantigen plasmid-based vaccine. Further studies are ongoing to correlate these differences to anti-tumor activity.