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In vivo T cell genetic engineering with melanoma-specific TCR and CAR

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SI/CTR Abstract

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Introduction: Adoptive cell transfer (ACT) using T cells genetically engineered to express tumor-specific T cell receptors (TCR) and Chimeric Antigen receptors (CAR) have demonstrated high remission rates in patients with advanced cancers. Targeting of metastatic melanoma with TCR-modified recombinant T cells showed clinically significant response in the majority of patients. However, due to certain drawbacks, this powerful strategy is not yet available for broad clinical application. We propose that in vivo genetic engineering approach may allow overcoming several drawbacks associated ACT and could convert it into generic and cost-effective modality to bring recombinant T cell therapies to general patient population.

Methods: Specifically, we suggested intradermal delivery of the recombinant TCR and CAR encoding plasmids into T cells combined with ΦC31 integrase-mediated gene transfer could be used to generate functional melanoma-specific T cells directly in tumor-bearing subjects. After injecting mice through in vivo electroporation, we observe the recruitment of T cells and plasmid incorporation.

Results: We obtained solid preliminary data showing that T cells genetically engineered to express tyrosinase-specific TCR in vivo can eliminate malignant lesions and produce tumor-specific immunologic memory through analysis of splenocytes. We also showed that this approach could be developed to generate CAR-expressing T cells to target malignant lesions.

Discussion: Our results support that In vivo T cell genetic engineering with melanoma specific TCR can have a significant effect on recruiting T cells and diminishing and

eliminating melanoma. This method could have significant improvements on reducing on-and-off target toxicities and costs but further studies must be done for future efficacy.