Deep TLR Primed™ T cells induce potent anti-tumor activity without systemic toxicity

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Deep TLR Primed™ T cells induce potent anti-tumor activity without systemic toxicity

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Abstract

TLR® agonists have been shown to augment immune responses in the tumor microenvironment (TME). The agonists work primarily through two mechanisms: antigen presenting cell (APC) engagement and enhancement followed by T cell co-stimulation. Herein, we screened several liposomal formulations containing TLR7/8 agonists, including Deep TLR® agonists capable of liposome encapsulation. Two different TLR7 agonists for both human and mouse T cells followed by systemic injection of antigen presenting cells (APCs), and by using Torque’s multi-targeted T cell (MTC) platform that primes the T cells against multiple tumor antigens. Hence, we screened several liposomal formulations containing two different TLR7 agonists for both in vitro agonist loading and release in mouse and human T cells followed by in vivo testing in a mouse melanoma model.

Introduction

Deep TLR Agonist

Loading onto antigen-specific CDB T cells

Deep TLR Primed T cell

Results

1. TLR agonists 1 and 2 are specific for TLR7?

2. Optimal liposome formulation maximizes agonist loading and extends drug release

3. Deep TLR loaded T cells retain viability and extend TLR agonist release

4. Deep TLR Primed™ T cells increase cell expansion and tumor control in vivo

Conclusions

• Torque’s Deep TLR Primed™ T cells released a potent, small-molecule agonist of TLR7 over an extended period of time.

• Two TLR7-specific agonists capable of liposome encapsulation were identified.

• Formulation optimization enabled high concentrations of two different TLR7 agonists to be loaded on both mouse and human T cells with extended release.

• The optimal liposomal formulation enabled encapsulation of high concentrations of TLR7 agonists loaded onto MTCs with minimal effect on viability and proliferative capacity.

• Deep TLR Primed™ T cells remain viable and release TLR agonist slowly over 10 days.

• Deep TLR Primed™ T cell expansion exceeds that of CD8 T cells alone or co-administered with systemic TLR7 agonist.

• ACT with Deep TLR Primed™ T cells provides a novel avenue to leverage the immune stimulating potential of TLR agonists for superior anti-tumor efficacy while avoiding systemic exposure and toxicities - key current bottlenecks to successful TLR therapy.

• In the future, agonist delivery via Deep-Primed™ tumor antigen-specific autologous T cells could target a wide variety of tumors and their distant metastases, enabling a new immunotherapy treatment.

References


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