Delivery of TLR7 agonists by Deep-Primed™ T cells induces immune activation and improves anti-tumor activity in mice while circumventing systemic toxicity

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Torque Deep TLR Primed™ T cell product

Introduction

TLR7 agonists boost immune responses in the tumor microenvironment (TME), primarily through dendritic cell (DC) engagement, enhancement of antigen presentation and T cell co-stimulation. Under these conditions, we designed a T cell mediated delivery system for TLR7 agonists that targets the TME and the lymphatic system to maximize efficacy while avoiding systemic toxicities. Torque’s Deep TLR Primed™ T cell technology enhances T cell function through tethering of immune modulators to the T cell before adoptive cell transfer (ACT) and uses Torque’s multi-armed agonist platform to prime the T cells against multiple tumor antigens. By transporting the immunomodulators to antigen-expressing tissues, Deep-Primed™ TMCs focus their effect on desired locations. Here, we show that Deep TLR Primed™ T cells delivering TLR7 agonists induce potent immune cell activation in the TME and elicit exquisite anti-tumor efficacy without overt toxicity.

Materials and experimental design

TLR7 agonists and several liposomal formulations were screened for optimal T cell tethering and release, measured by HPLC.

Key findings

- Torque’s Deep TLR Primed™ T cells release a potent small molecule agonist of TLR7 over an extended period of time and improves anti-tumor activity in mice while circumventing systemic toxicity
- Deep TLR Primed T cell technology increases T cell expansion
- Antigen presentation and T cell co-stimulation
- Deep TLR Primed T cells promote tumor growth inhibition and extend host survival
- Weight change
- Cytokine release kinetics

Figure 1. Deep TLR Primed T cells release a potent TLR7 agonist over an extended period of time

Figure 2. Deep TLR Priming increases T cell expansion in vivo and reduces PD-1 expression

Figure 3. TLR7 agonist delivery enriches pDCs in draining LNs as well as endogenous CD8 T cells and MDSCs in tumors

Figure 4. Deep TLR Primed T cells promote tumor growth inhibition and extend host survival

Figure 5. ACT of Deep TLR Primed T cells exhibits low potential toxicity

Artificial T cell immune therapy has the potential to be efficacious and well tolerated.

1. Deep TLR Primed T cells contain TLR7 agonist loaded liposomes and display slow payload release over time

2. Deep TLR Priming increases T cell expansion in vivo and reduces PD-1 expression

3. TLR7 agonist delivery enriches pDCs in draining LNs as well as endogenous CD8 T cells and MDSCs in tumors

4. Deep TLR Primed T cells promote tumor growth inhibition and extend host survival

5. Deep TLR shows low potential toxicity

- Torque’s Deep TLR Primed T cells release a potent small molecule agonist of TLR7 over an extended period of time and improves anti-tumor activity in mice while circumventing systemic toxicity
- Deep TLR Primed T cell technology increases T cell expansion
- Antigen presentation and T cell co-stimulation
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Figure 1. ACT of Deep TLR Primed T cells exhibits low potential toxicity

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