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

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Total number of authors: 15

Publication date: 2019

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
Deep TLR Primed™ T cells induce potent anti-tumor activity without systemic toxicity

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**Abstract**

TLR7 agonists have been shown to augment immune responses in the tumor microenvironment (TME). The agonist work primarily through two mechanisms: antigen presenting cell (APC) engagement and enhancement followed by T cell co-stimulation. However, multiple TLR agonists, including TLR7/8 agonists, have displayed considerable toxicities upon stimulation. Herein, we screened several liposomal formulations containing TLR7/8 agonists, have displayed considerable toxicities upon stimulation. (APC) engagement and enhancement followed by T cell co-stimulation. TLR7 agonists have been shown to augment immune responses. The authors present a novel approach to load TLR agonists onto tumor cells in vitro and to extend TLR agonist release in vivo, which is beneficial for therapeutic interventions in the TME.

**Introduction**

Deep TLR Agonist

**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 TLR agonists to be loaded onto both mouse and human T cells with extended release.
- The optimal liposomal formulation enabled encapsulation of high concentrations of TLR agonists into liposomes 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 distinct metastases, enabling a new immunotherapy approach.

**References**

3. Dowling D. Recent Advances in the Discovery and Delivery of TLR7 Agonists as Vaccine Adjuncts. ImmunoHorizons 2018;0152625.

**Acknowledgments**

We would like to thank our Torque colleagues for productive discussions and critiques.