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

Deep TLR Primed T cell

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

Key findings
- Torque’s Deep TLR Primed T cells release a potent small molecule agonist of TLR7 over an extended period of time.
- Deep TLR Primed T cells significantly improve tumor growth inhibition and host survival over controls in the murine B16-F10 model.
- Deep TLR Primed T cell expansion exceeds that of CD8 T cells alone or co-administered with a TLR7 agonist. PD-1 downregulation suggests reduced exhaustion of Deep TLR Primed T cells vs. controls.
- Deep TLR-mediated agonist delivery increased pDCs in draining lymph nodes and endogenous CD8 T cells in tumors, consistent with the known effects of TLR7 agonists in vivo (Mouries et al. 2008).
- Deep TLR-mediated agonist delivery increased MDSC content in the TME which may be beneficial given TLR7 agonists are known to convert MDSCs into functional APCs (Spinetti et al. 2016).
- Deep TLR Primed T cells caused no significant weight loss. Transient plasma levels of pro-inflammatory cytokines (TNFα and IL-6 not shown) remained below 5% of known toxic levels (Soros et al. 2014, Baird et al. 2009, Tatedo et al. 1996). This suggests that our Deep TLR Primed T cell therapy has the potential to be efficacious and well tolerated.