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

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Publication date:
2019

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

Citation (APA):
Herein, we screened several liposomal formulations containing a platform that primes the T cells against multiple tumor antigens (ACT), and by using Torque’s multi-systemic administration.

TLR7/8 agonists, have displayed considerable toxicities upon systemic administration. To circumvent this problem, we loaded onto CD8 T cells Deep TLR agonist 2. However, multiple TLR agonists, including TLR7 agonist and TLR8 agonist for various therapy groups.

Figure 2. TLR Agonist release from Deep TLR Primed MTCs in vitro. MT cells were loaded with Deep TLR Priming process occurs via peptide-T cell interaction by downregulation of class II MHC. For example, the optimal liposomal formulation enabled encapsulation of different TLR 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.

Figure 1. A) Cells expressing human TLR 7 or 8 over-expressed tumor-specific antigens on the cell surface and intracellularly. After adding different concentrations of TLR agonist 1 or TLR agonist 2, in the presence of liposome formulation, the cells were cultured for 24 h. B) Tumor activity without systemic toxicity. Mouse T cells expansion exceeds that of CD8 T cells alone or co-administered with systemic TLR7 agonist.


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 TLR7 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 strategy.

References

3. Development of Best Antennas to Discover and Deliver of TLR7 Agonists as Vaccine Adjuvants. ImmunoHorizons 2018:2.156-167

Acknowledgments

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