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

Westcott, Nathan; Boesch, Austin; Rybakin, Vasily; Hwang, Ji Young; Jørgensen, Kira; Lassen, Rasmus; Kræmer, Martin; Bak, Martin; Veiga, Gael; Bruun, Jonas

Publication date: 2019

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

Citation (APA): Westcott, N., Boesch, A., Rybakin, V., Hwang, J. Y., Jørgensen, K., Lassen, R., ... Andresen, T. L. (2019). Deep TLR Primed™ T cells induce potent anti-tumor activity without systemic toxicity. Poster session presented at AACR Special Conference on Tumor Immunology and Immunotherapy, Boston, United States.
Deep TLR Primed™ T cells induce potent anti-tumor activity without systemic toxicity

Nathan Westcott¹, Austin Boesch¹, Vasily Rybakin¹, Ji Young Hwang¹, Kira Jørgensen², Rasmus Lassen¹, Martin Kraemer², Martin Bak³, Gael Veiga³, Jonas Bruun¹, Carlos Tassa¹, Harrison Rodts¹, Manny Sequeira¹, Karsten Sauer¹, Thomas L. Andresen¹

¹Torque Therapeutics, Cambridge, MA ²Technical University of Denmark, Lyngby, Denmark

Introduction

TLR7 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. However, multiple TLR agonists, including TLR7/8 agonists, have displayed considerable toxicities upon stimulation. TLR7 agonists have been shown to augment immune responses primarily through two mechanisms: antigen presenting cell in the tumor microenvironment (TME).

Abstract

Deep TLR Agonist - Boston, MA

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 TLR agonist 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

3. Dowling D. Recent Advances in the Discovery and Delivery of TLR7/8 Agonists as Vaccine Adjuvants. ImmunoTherapeutics 2018: 1405-1417

Acknowledgments

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