**Introduction**

- Accumulating evidence suggests that low baseline tumor infiltrating lymphocytes (TILs) are predictive for poor response to checkpoint inhibitor immunotherapies, thus agents designed to specifically activate and expand TILs may improve the overall success and utility of checkpoint inhibitor therapies in patients with low TILs.
- Interleukin-2 (IL-2) is a cytokine that activates and expands tumor killing lymphocytes, but also potently activates suppressive T regulatory cells (Tregs) by binding to the heterotrimeric IL-2Rαβγ.

**Objectives**

In this pre-clinical study, we investigated whether NKTR-214 can promote expansion and function of vaccination-induced, tumor specific effector CD8+ T cells using the murine B16 melanoma model. We also studied how NKTR-214 impacts the localization of effector CD8+ T cells and Tregs to tumor and spleen.

**NKTR-214 improves anti-tumor efficacy of peptide vaccines**

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- Vaccine formulation
- Transfer of TCR transgenic pmel-1 CD8+ T cells
- Treatment repeated till experimental end point

**NKTR-214 impacts the localization of Pmel-1 cells**

Tumor size

- Tumor Induction
  - 30,000 B16 wild type cells
- Tumor size
  - Days 6, 5, 4, 3, 2

Pmel-1 CD8+ T cells

- CD25+ Foxp3+ Tregs
- CD25+/Foxp3- T cells
- PMel-1 (% of CD8+ T cells)
- Number of Treg/spleen: Tumor/spleen
- Number of TILs (CD8+ or CD4+ T cells)
- Ratio CD8+/CD4+ T cells

**Conclusions**

- NKTR-214 efficiently synergized with vaccination, potently suppressing tumor growth and improving survival of mice compared to vaccination with IL-2.
- NKTR-214 significantly enhanced pmel-1 CD8+ T cells numbers in tumor and spleen.
- NKTR-214 specifically decreased numbers of immune-suppressive Tregs in the tumor while maintaining their numbers in spleen.
- Despite the induction of very strong CD8+ T cell responses and anti-tumor activity, no gross toxicity was observed.

**References**