Thomas Jefferson Univers
Jefferson College of Biomedical Sciences

Virus-Specific CD8+ T cells Infiltrate Melanoma Lesions and Remain Functional Despite being PD-1^{hi}

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Poster # 78

Presenter Disclosure Information

Dan A. Erkes, PhD Candidate

The following relationships exist related to this presentation:

P.I. Christopher M. Snyder, PhD has a financial stake in UbiVac CMV

CD8+ Tumor Infiltrating Lymphocytes (TIL)

- Embedded in the tumor tissue
- **Positive correlation between CD8+ TIL and prognosis for several cancers or outcomes of therapies**
- **Generally assumed that CD8+ TIL are tumor specific**
  - Virus-specific CD8+ TIL?

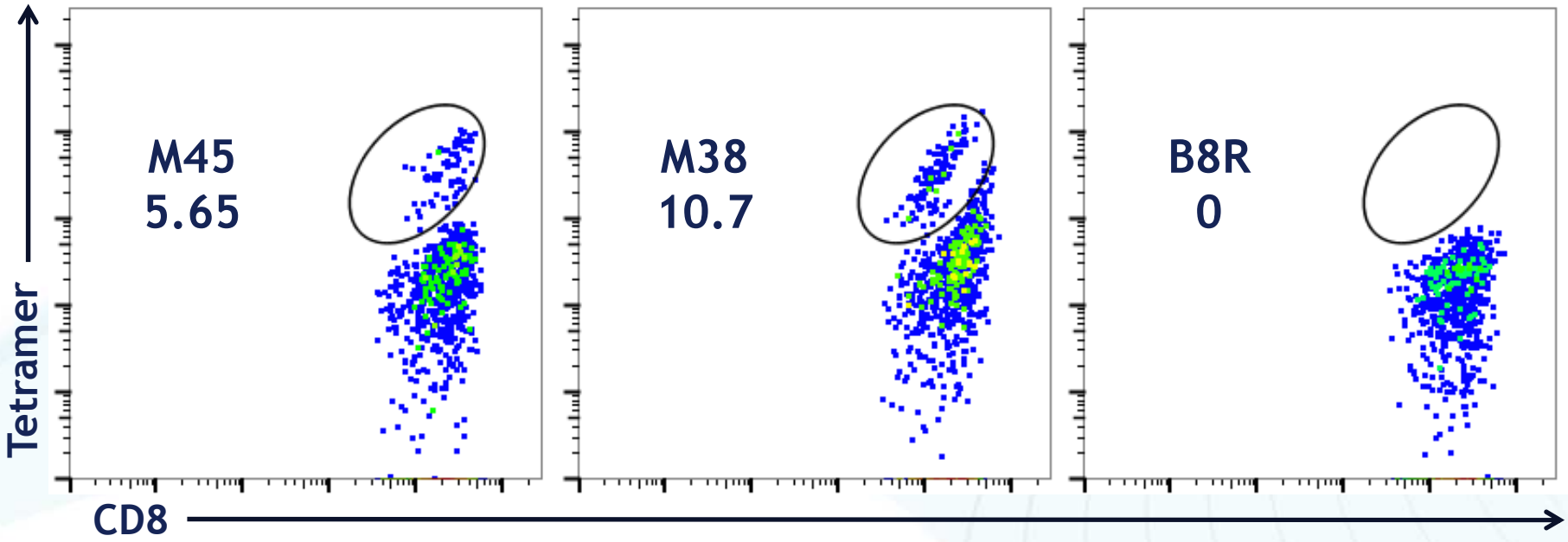
Herpes Infections

- Most people in the world are latently infected with multiple herpes viruses
- Latent herpes infections require continuous immune surveillance

- **Cytomegalovirus (CMV) is a ubiquitous ß-herpes virus**
  - 60-100% of people infected
- Has been recently used as a vaccine vector for infectious disease and melanoma

Murine CMV induced virus-specific CD8+ Tumor Infiltrating Lymphocytes (TIL)

- D0: Subcutaneously implanted B16s
- D5: Infected with MCMV



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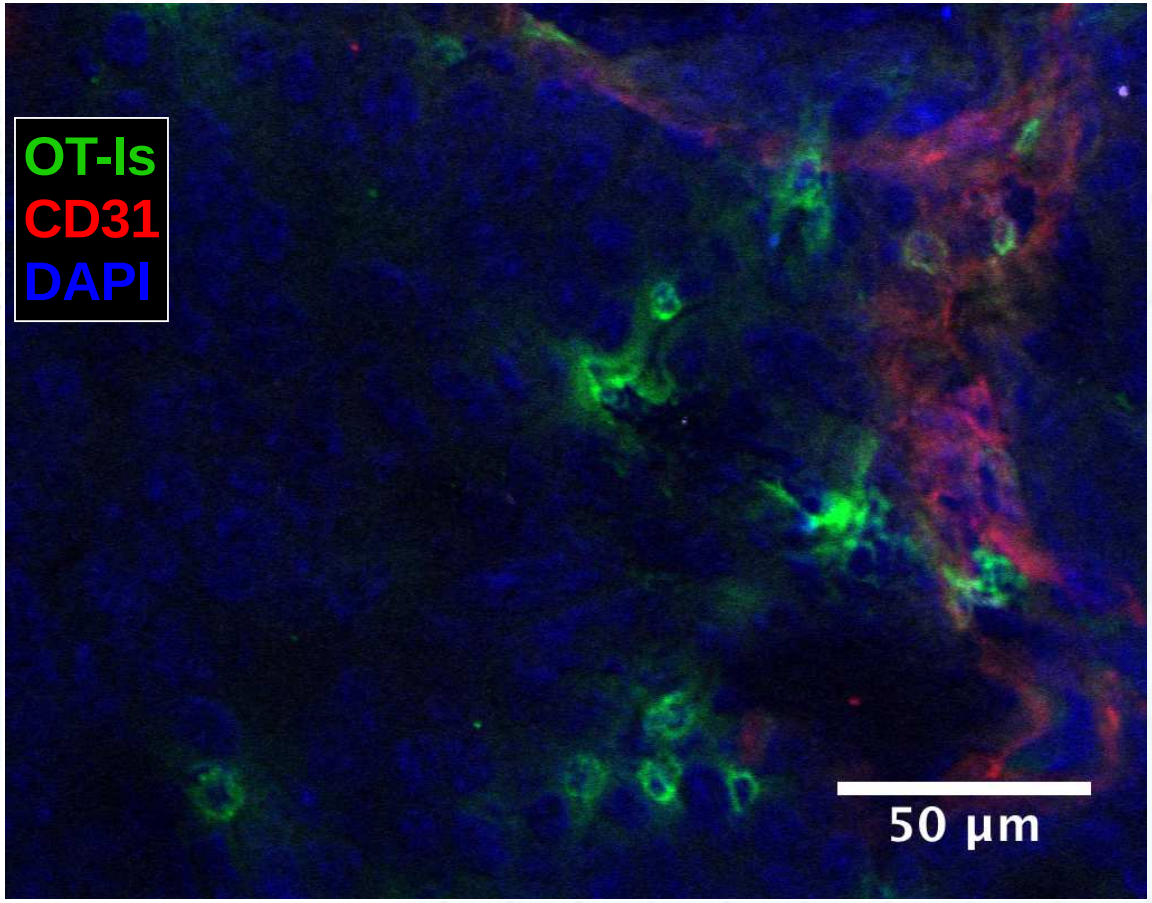
MCMV-specific CD8+ T cells are embedded in the tumor tissue

Switched to the OT-I system

- D-1: Gave 1,000 OT-Is
- D0: Subcutaneously implanted B16s
- D5: Infected with MCMV-Ova
- D12: Histology



Also confirmed with intravascular CD8 staining

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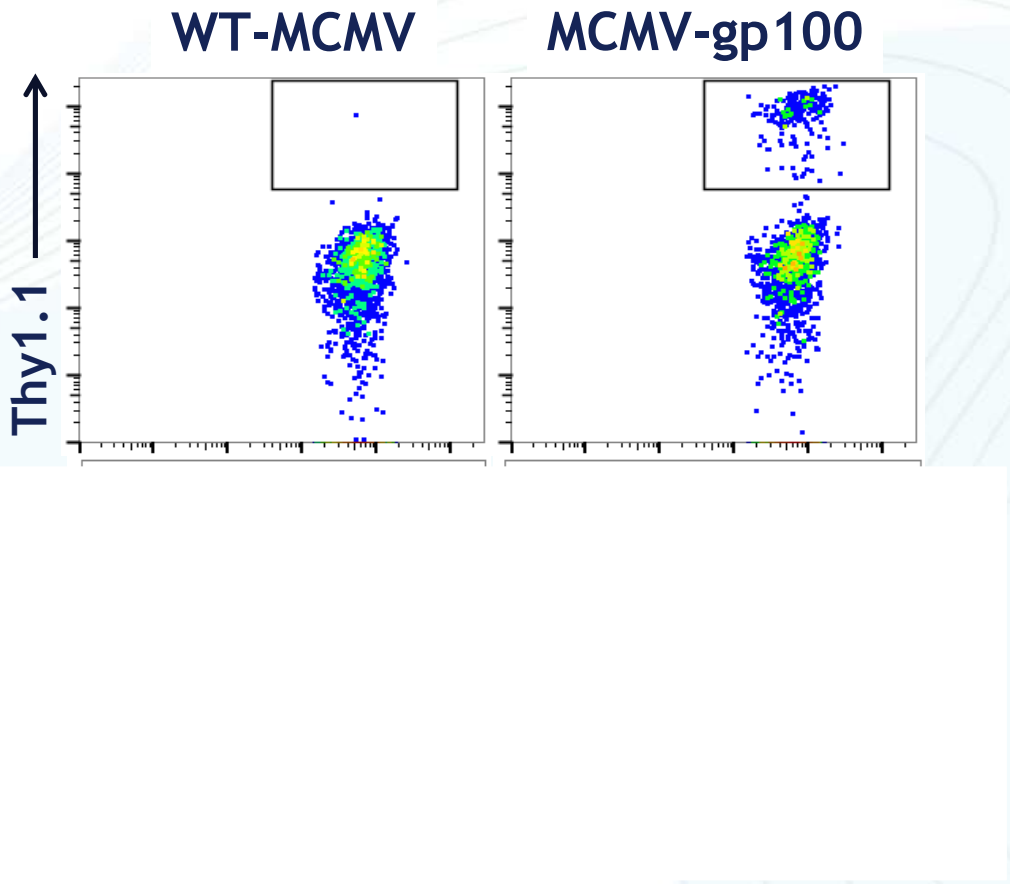
MCMV-gp100 induced Tumor-specific CD8+ Tumor Infiltrating Lymphocytes (TIL)

- D-1: Gave 50,000 Pmel-Is
- D0: Subcutaneously implanted B16s
- D5: Infected with MCMV-gp100



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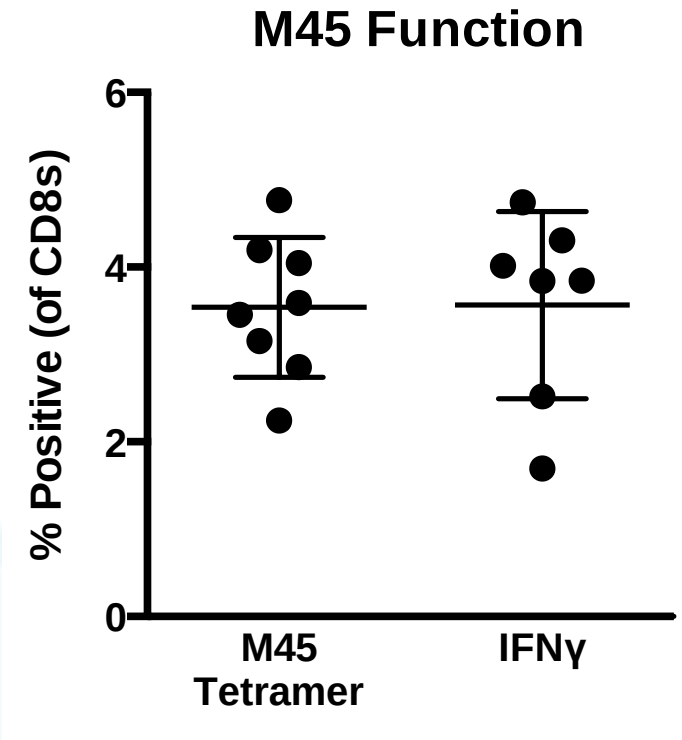
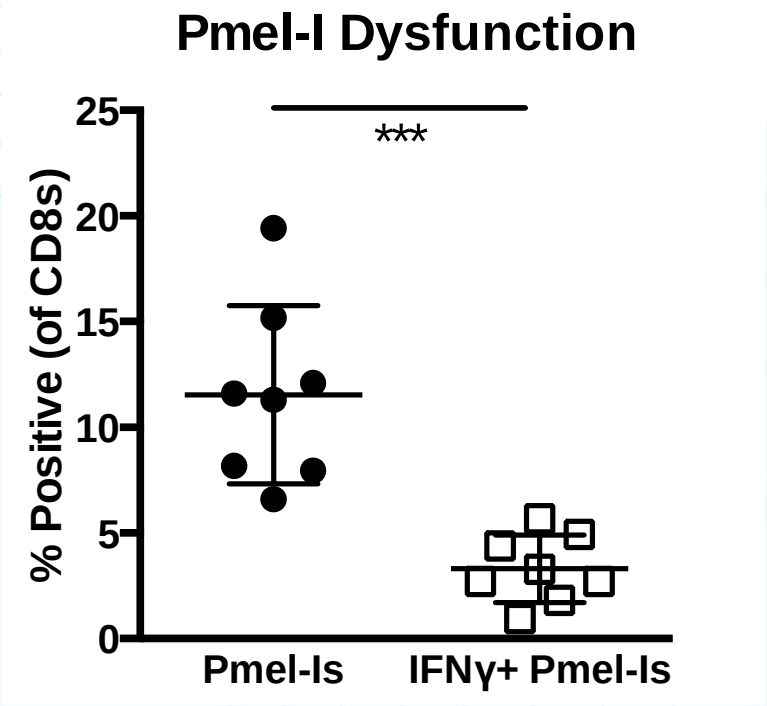
MCMV-specific TIL are functional despite PD-1^{hi} expression





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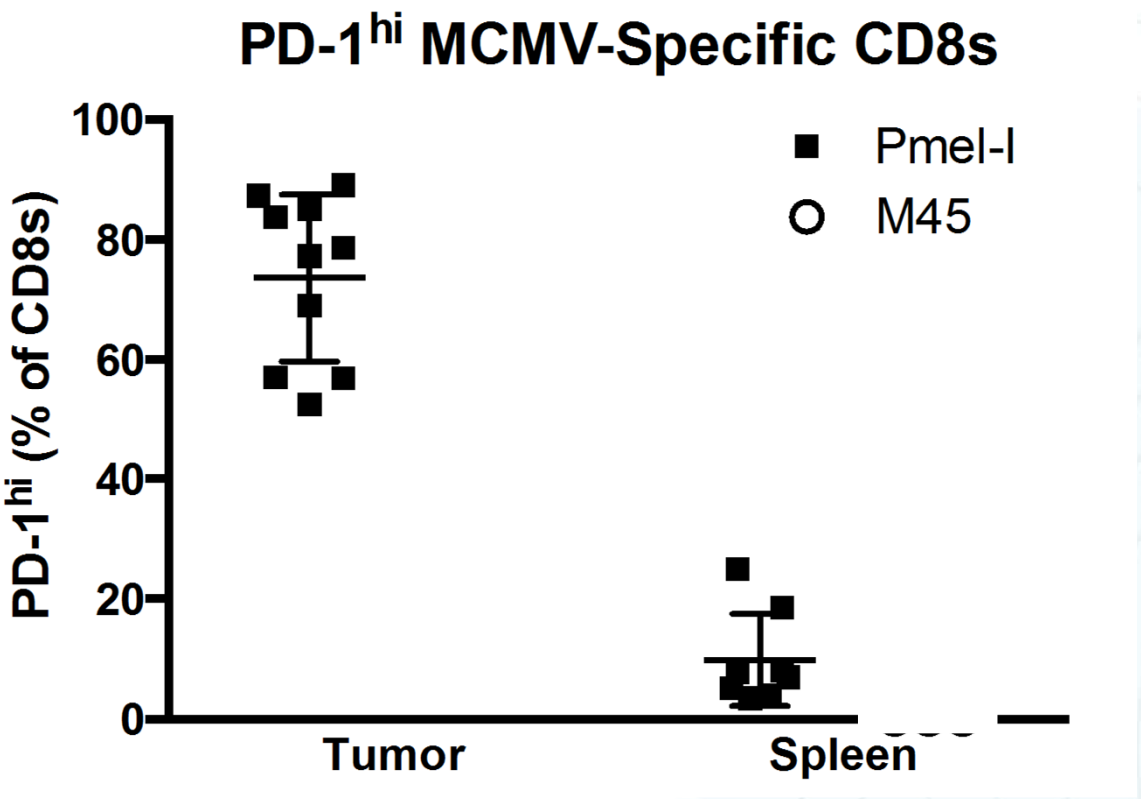
MCMV-specific TIL are functional despite PD-1^{hi} expression



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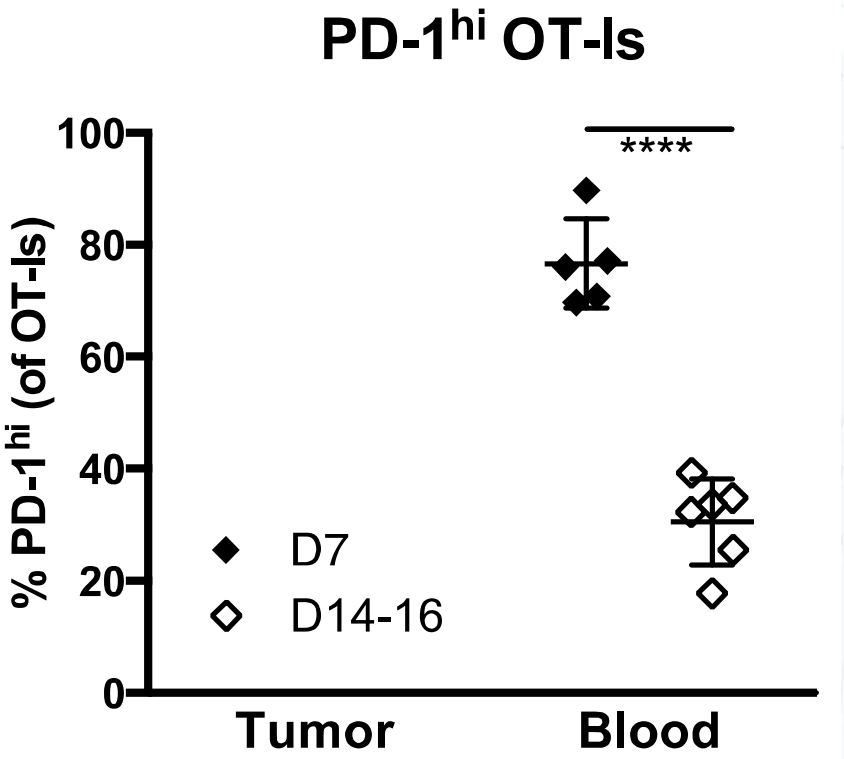
PD-1^{hi} expression is maintained in the tumor

Went back to the OT-I system



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Conclusions thus far

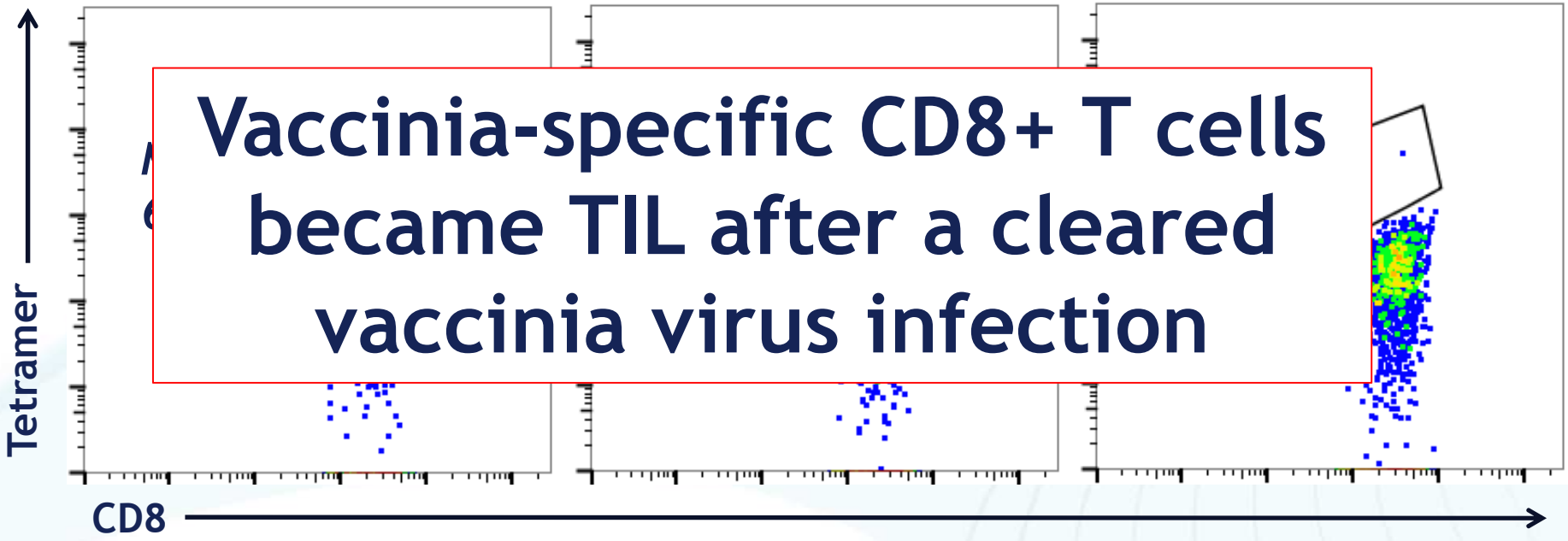
- MCMV-specific CD8+ T cells become TIL
  - Embedded in the tumor tissue
- MCMV-specific CD8+ TIL are functional despite PD-1^{hi} expression
  - PD-1 expression is maintained in the tumor

Vaccinia-specific CD8+ T cells become TIL, and are fully functional despite PD-1^{hi} expression after Vaccinia virus infection

MCMV-specific TIL are present during latent infections and are fully functional

Latent MCMV infection

- We infected mice with MCMV-K181 for > 12 weeks
- Gave mice B16 Tumors



Vaccinia-specific CD8+ T cells became TIL after a cleared vaccinia virus infection

All functional and embedded in the tissue

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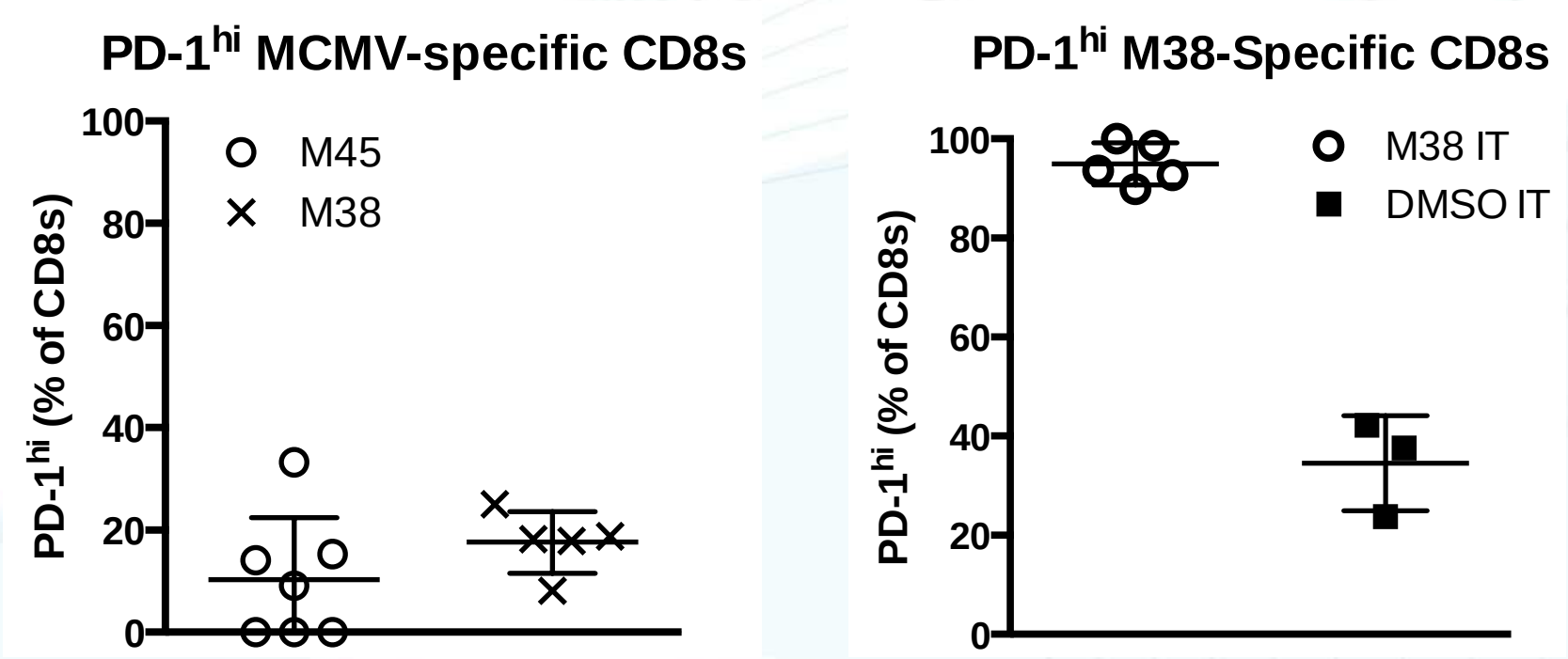
PD-1 expression of TIL controlled in antigen-dependent manner



Cells remain functional, despite PD-1^{hi} expression

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Take home messages

- TIL are not always tumor-specific
- Virus-specific T cells can become TIL during acute, latent, or cleared infections
  - Function independent of PD-1 expression

Future Questions

- Does this occur: In humans? In other tumors? With other infections?
- Does this impact prognoses, diagnostic TIL assays, or outcomes of therapy?

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