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& Convention Center



Society for Immunotherapy of Cancer

SITC
2017

PD-L1 expression on malignant cells is no prerequisite for checkpoint therapy

Jan Willem Kleinovink



Society for Immunotherapy of Cancer

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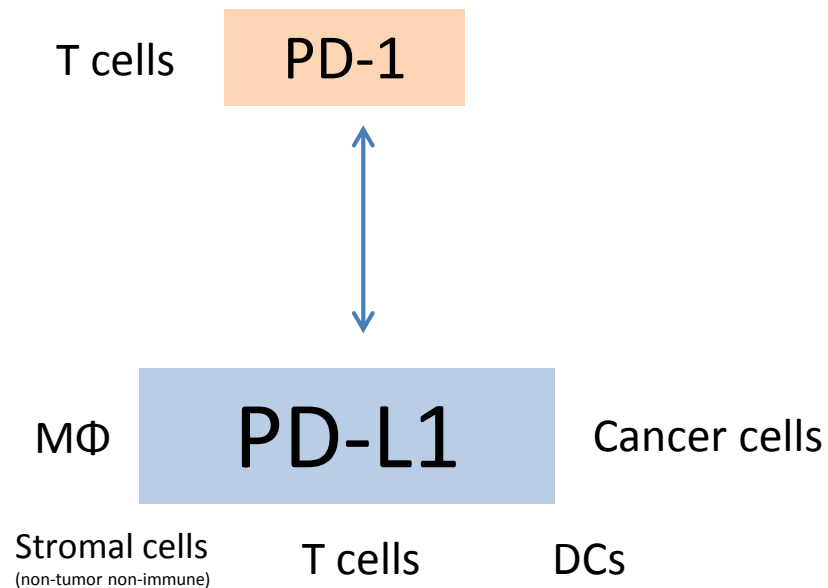
Presenter Disclosure Information

Jan Willem Kleinovink

The following relationships exist related to this presentation:

<No Relationships to Disclose>

The PD-1/PD-L1 signaling axis in cancer



Therapeutic efficacy of PD-1/PD-L1 blockade correlates with

- mutational load
- presence of tumor-infiltrating T cells
- PD-L1 expression *in the tumor*

└─ Which PD-L1 expression matters?

Intratumoral cell-specific PD-L1 expression in response to PD-1/PD-L1 blockade

Clinical

Herbst *et al.*, Nature 2014

“...across multiple cancer types, responses to anti-PD-L1 were observed in patients with tumors expressing high levels of PD-L1, **especially** when PD-L1 was expressed by tumor-infiltrating immune cells”



IHC assay separately scoring PD-L1 expression on cancer cells and immune cells (Ventana sp142)

Goal:

dissect the role of PD-L1 expression on tumor vs non-tumor cells in PD-1/PD-L1 blockade

Preclinical

Mouse tumor models responsive to PD-1/PD-L1 blockade

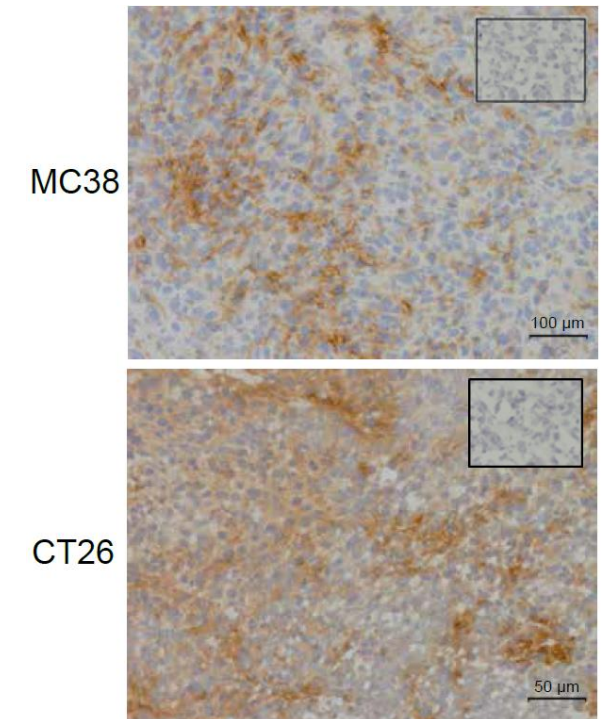
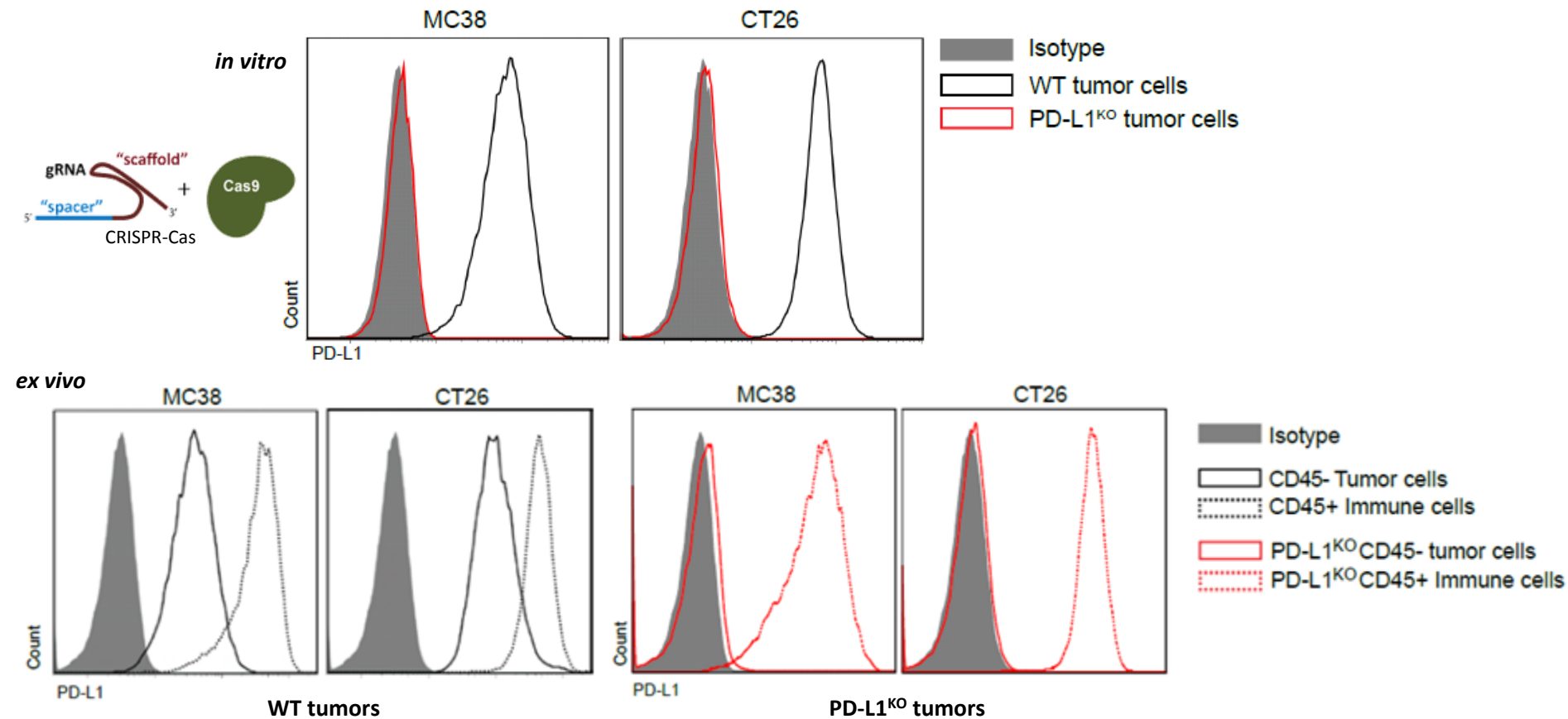


MC38
BL/6 mice

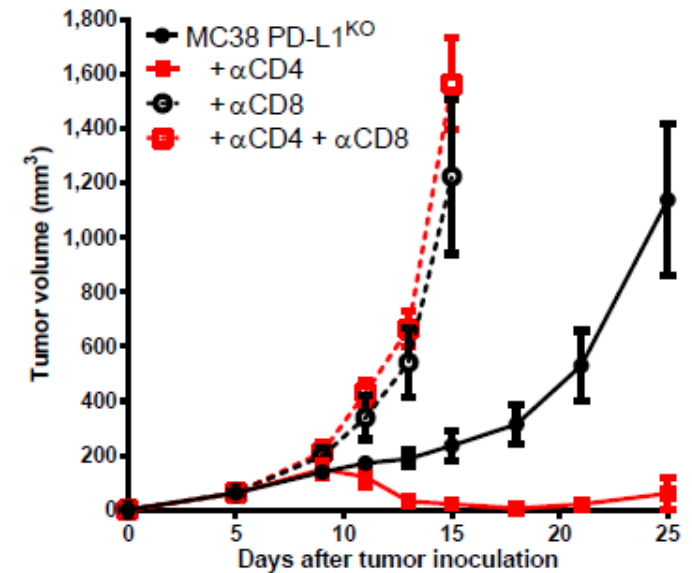
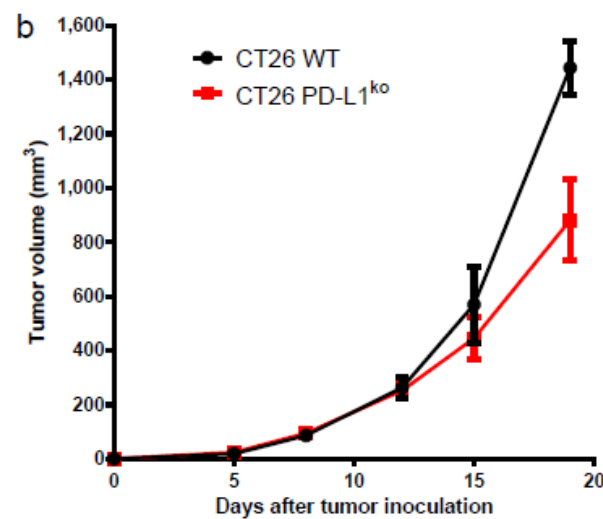
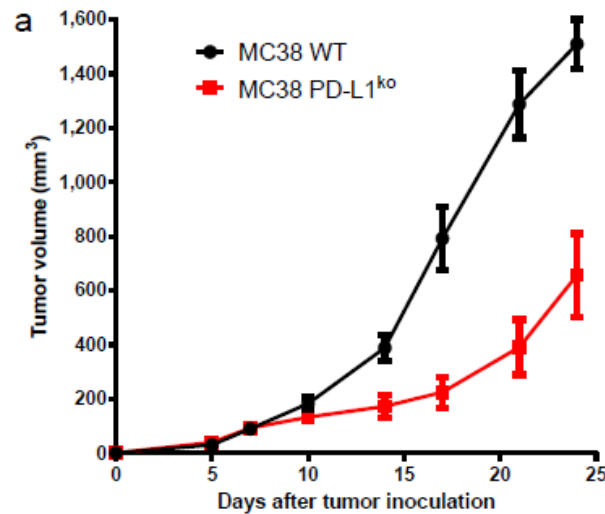
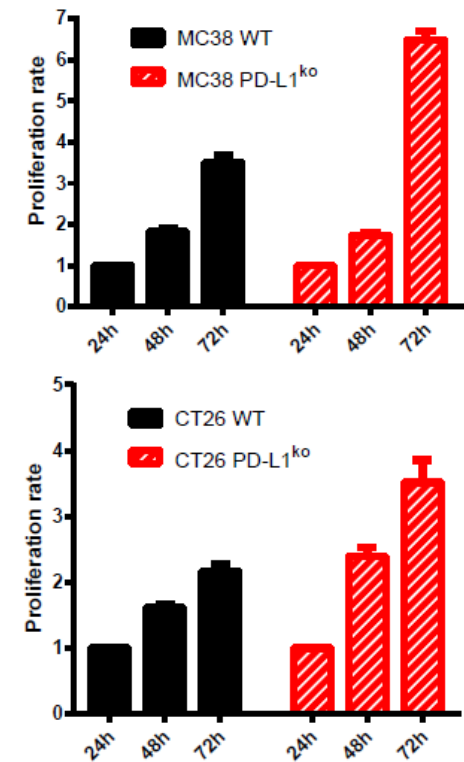
CT26
Balb/c mice



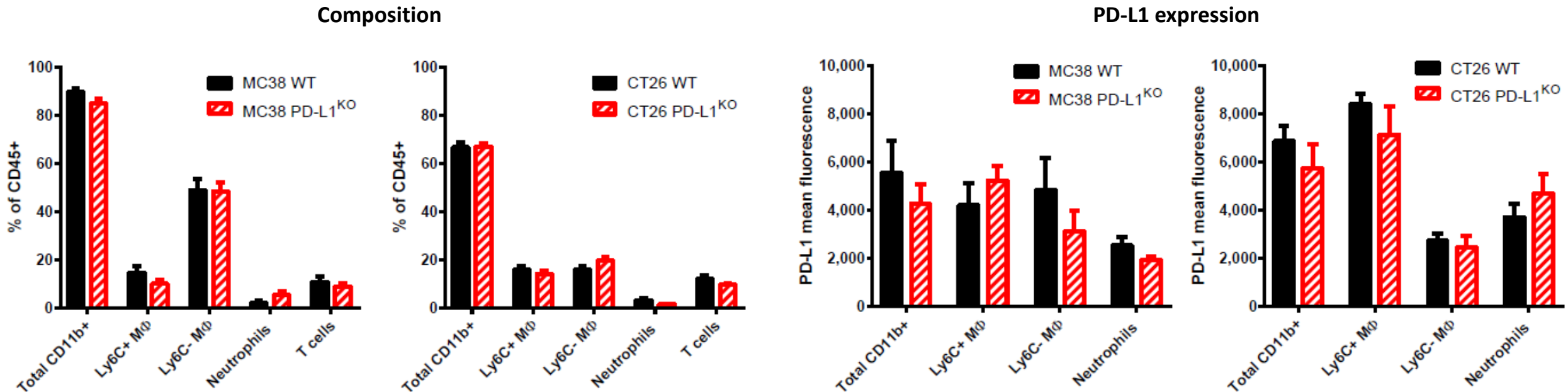
PD-L1 is expressed on both tumor cells and infiltrating immune cells



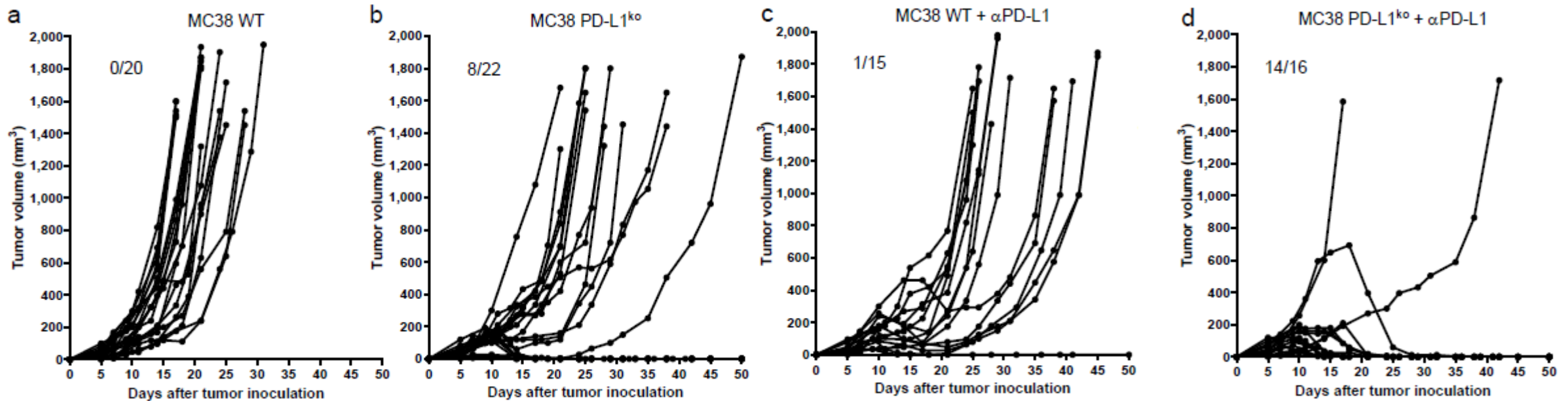
PD-L1 on cancer cells suppresses CD8+ T cell-mediated immune control



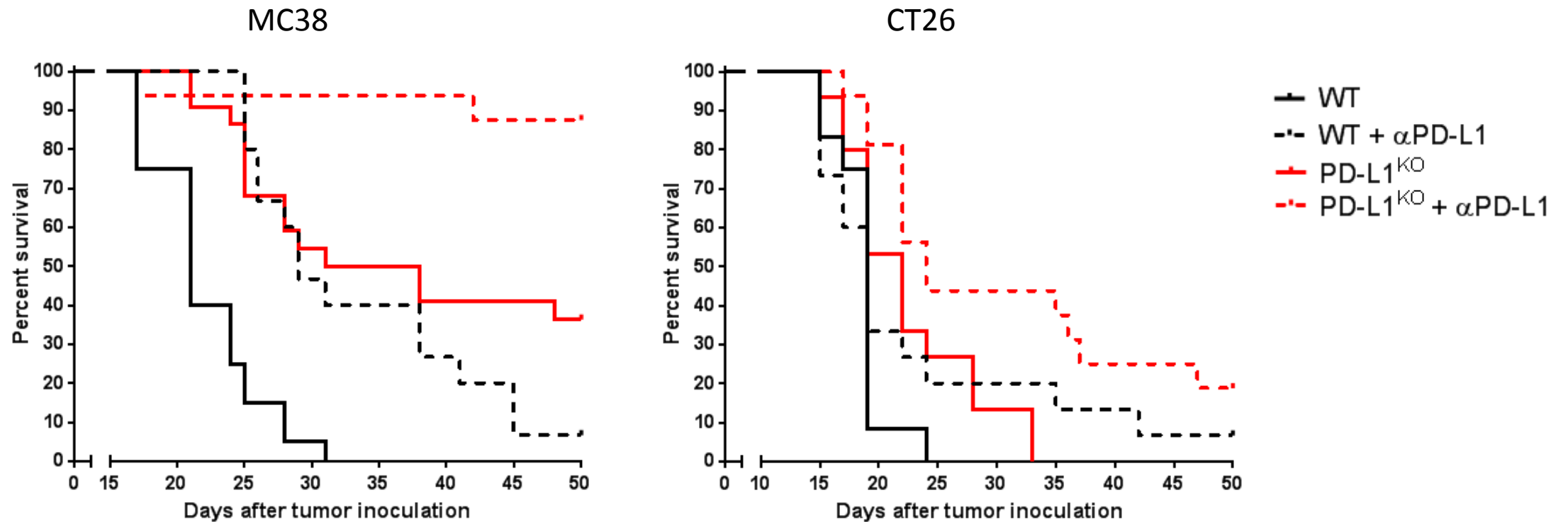
Comparable immune infiltrate and PD-L1 expression in WT and PD-L1^{KO} tumors



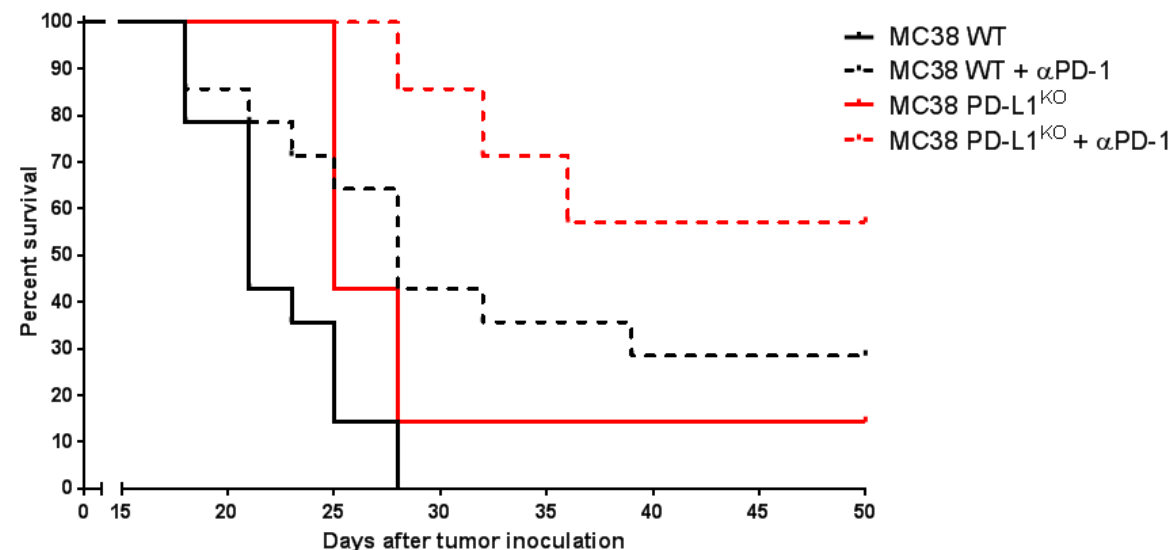
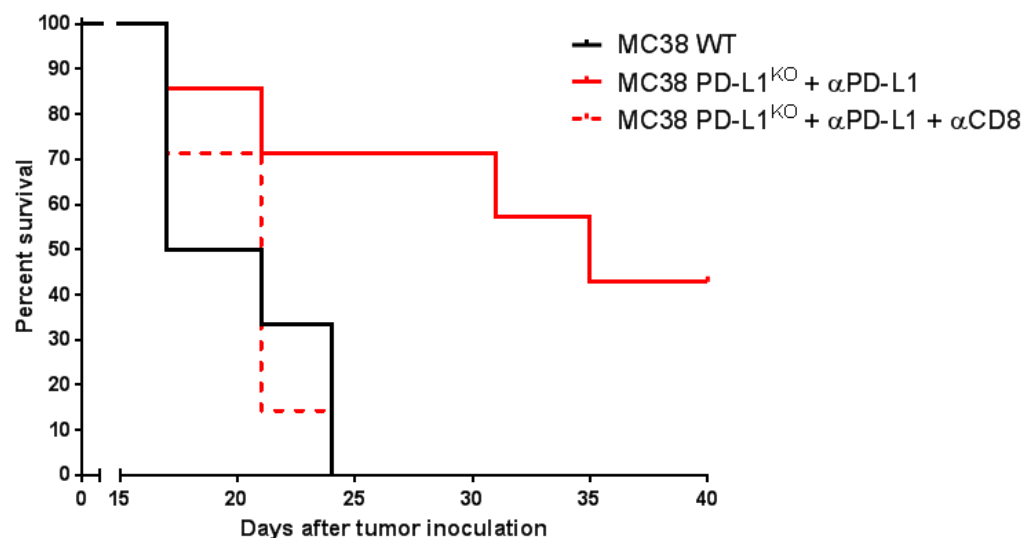
PD-L1 blockade is effective against PD-L1^{KO} tumors



PD-L1 blockade is effective against PD-L1^{KO} tumors



CD8 T cells mediate the therapeutic effect of blocking host PD-L1/PD-1 signaling

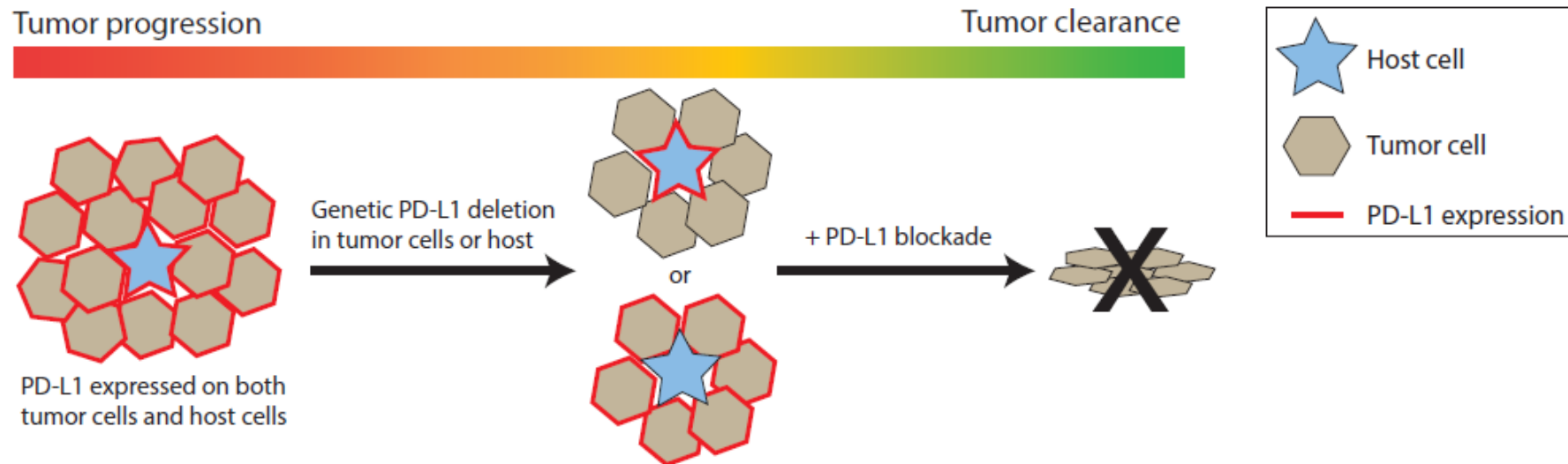


Lessons and Take Home Messages

- PD-L1 on tumor cells and infiltrating immune cells both contribute to tumor outgrowth by suppressing CD8 T cells
→ Disrupting PD-L1 signaling on tumor or non-tumor cells leads to CD8 T cell-mediated tumor control

Experimental evidence supporting the clinical observation:

→ PD-1/PD-L1 blockade can have strong effect in tumors lacking PD-L1 expression on malignant cells



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