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Society for Immunotherapy of Cancer



ADT-mediated IL-8 Promotes Myeloid Infiltration and Prostate Cancer Progression

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New York, 7th November 2019



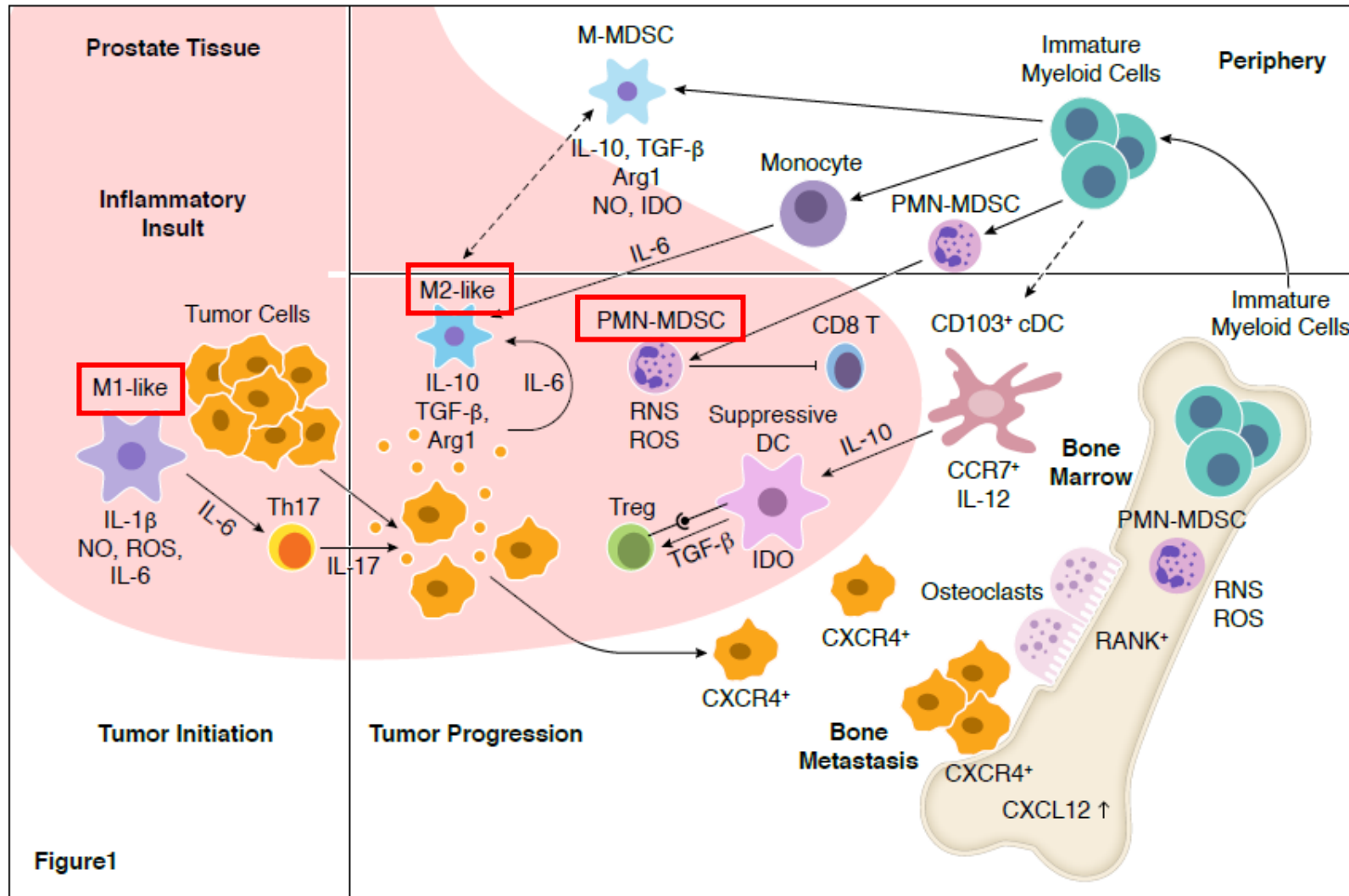
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Disclosure

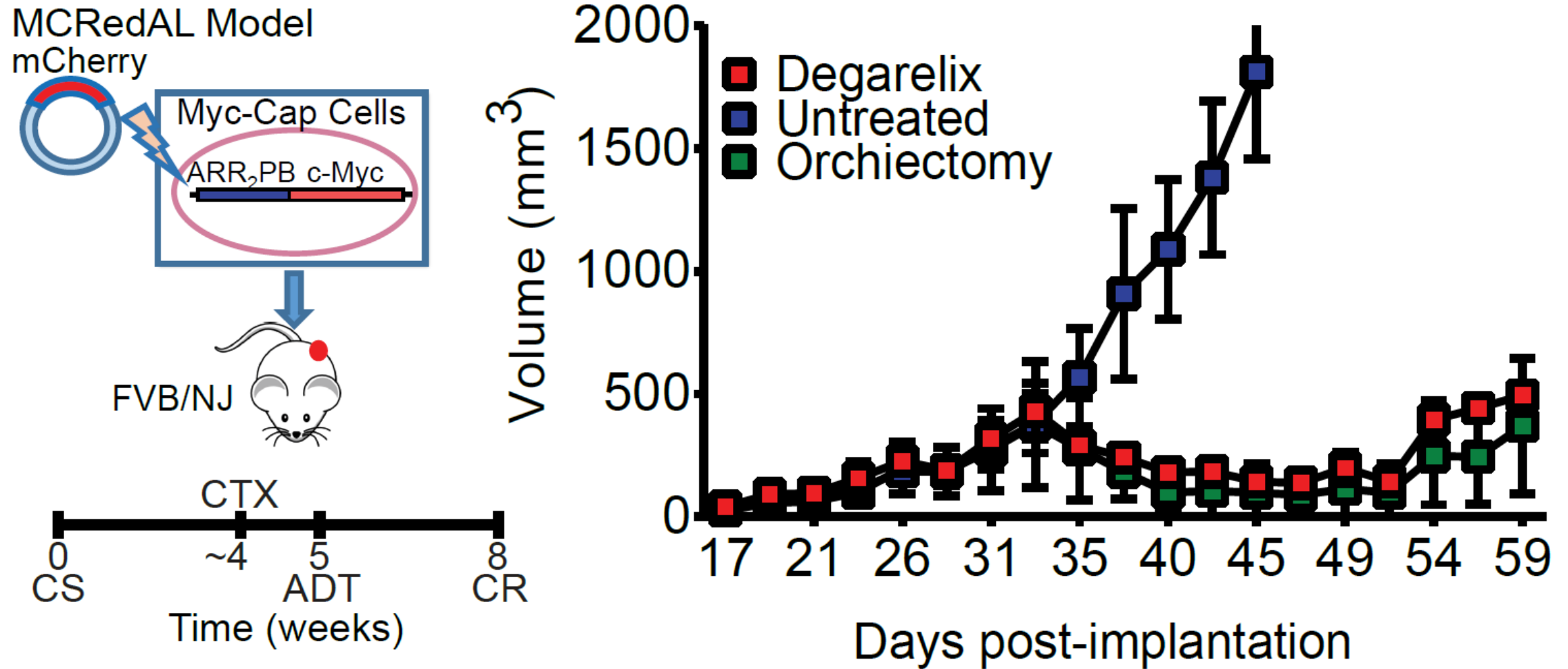
- ZALB Declares no competing interests.
- US Provisional Patent Application (No. 62/809,060) was filed.

Myeloid Cells Infiltration of Prostate Cancer



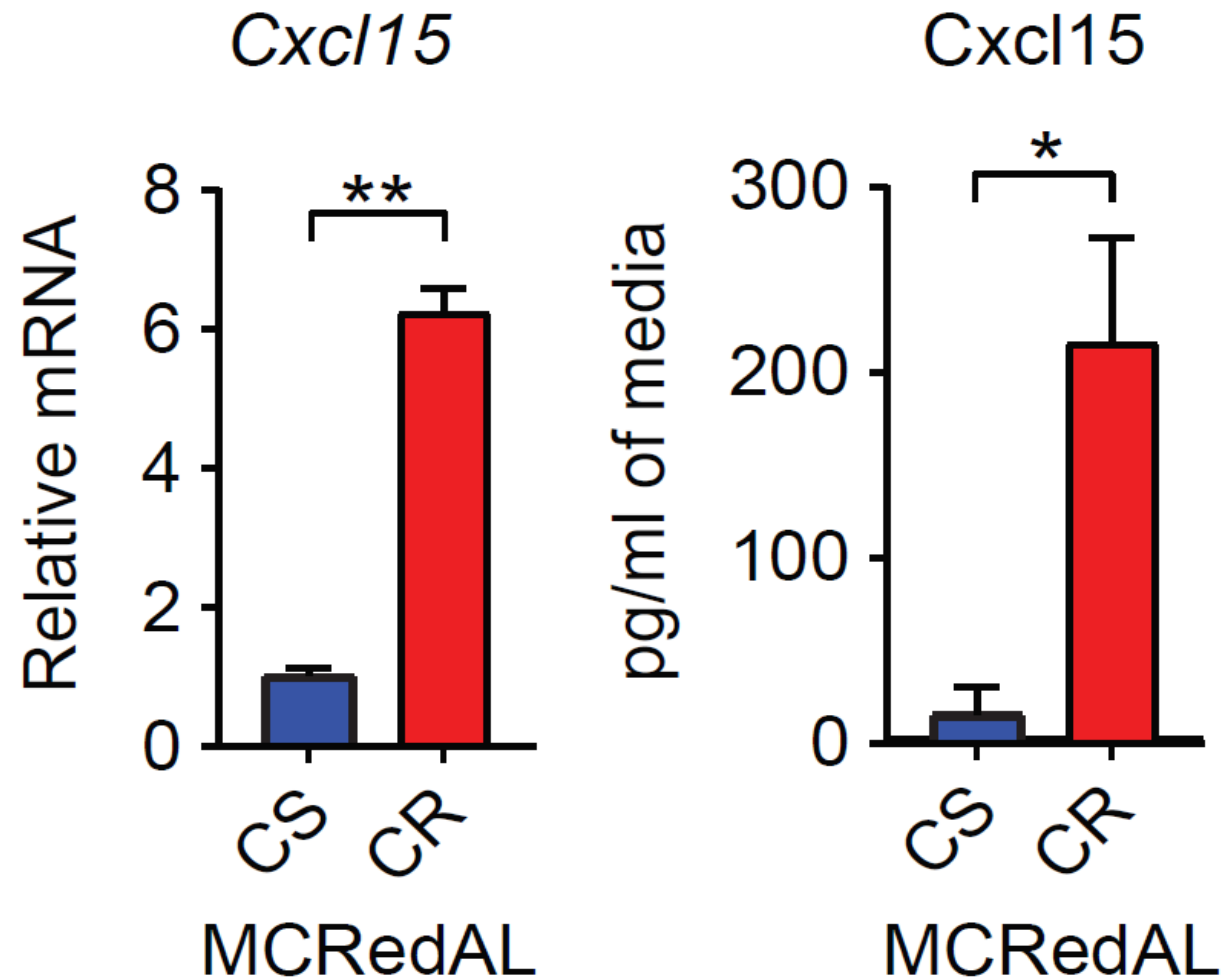
Lopez Bujanda Z.A. and Drake C.G., JLB, 12 (2017).

MCRedAL Recapitulates the Response ADT



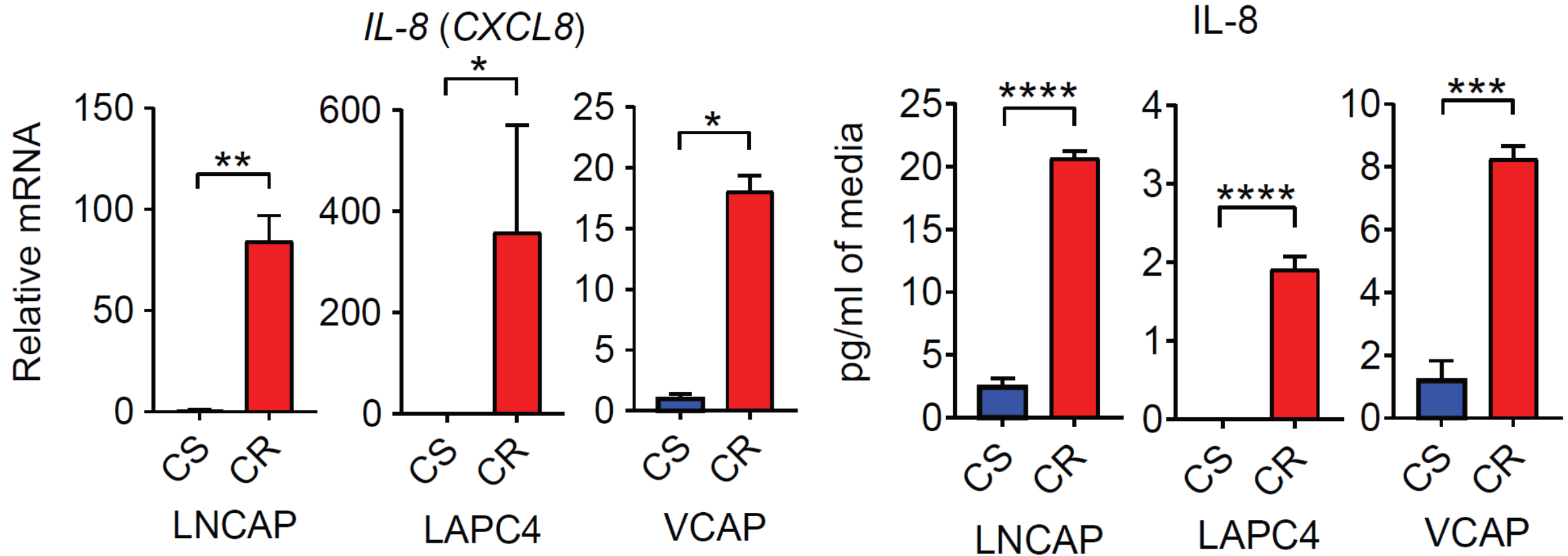
Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

Cxcl15 (mIL-8) Transcript and Protein Expression Increases Following ADT



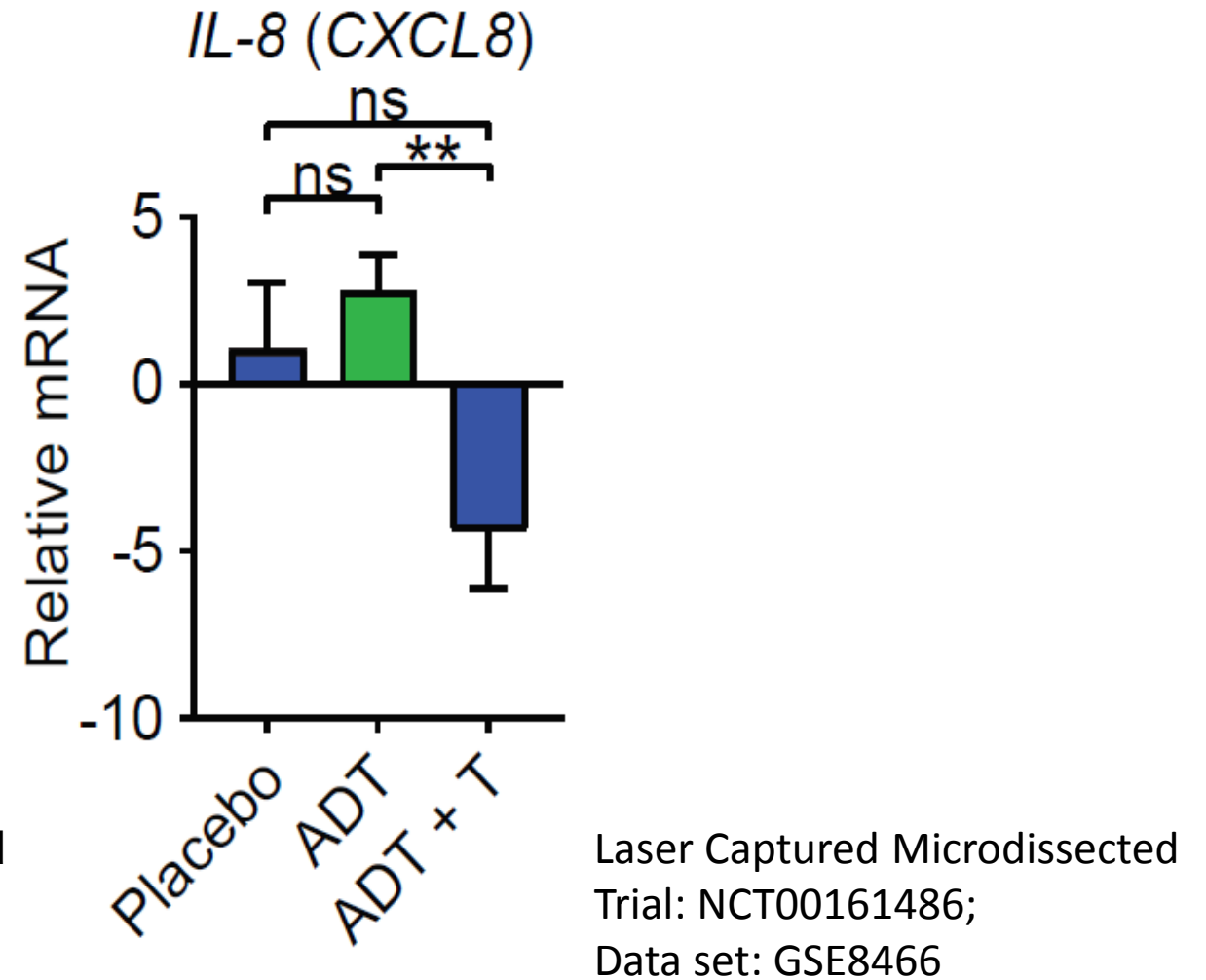
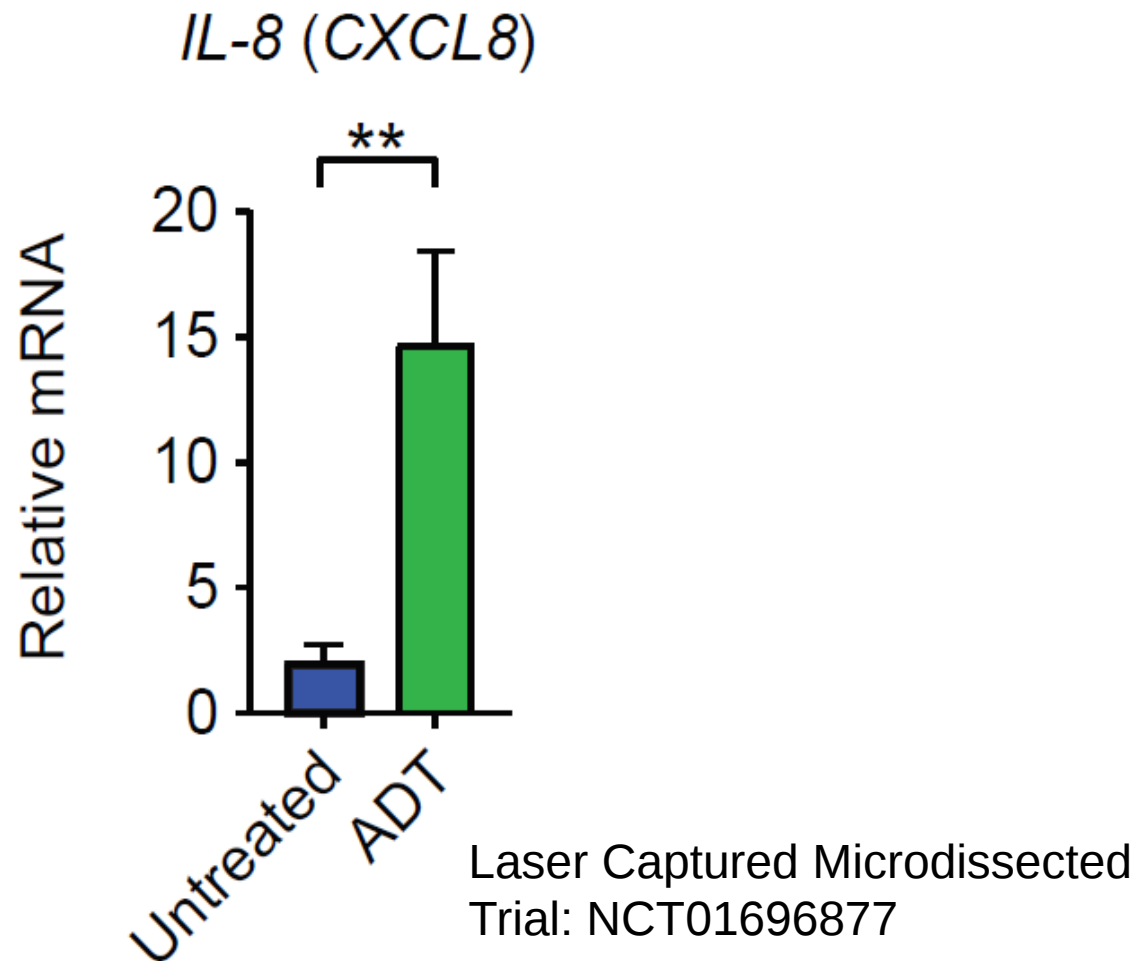
Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

Human CR Cells Express Higher Levels of IL-8 Than CS Isogenic Counterparts



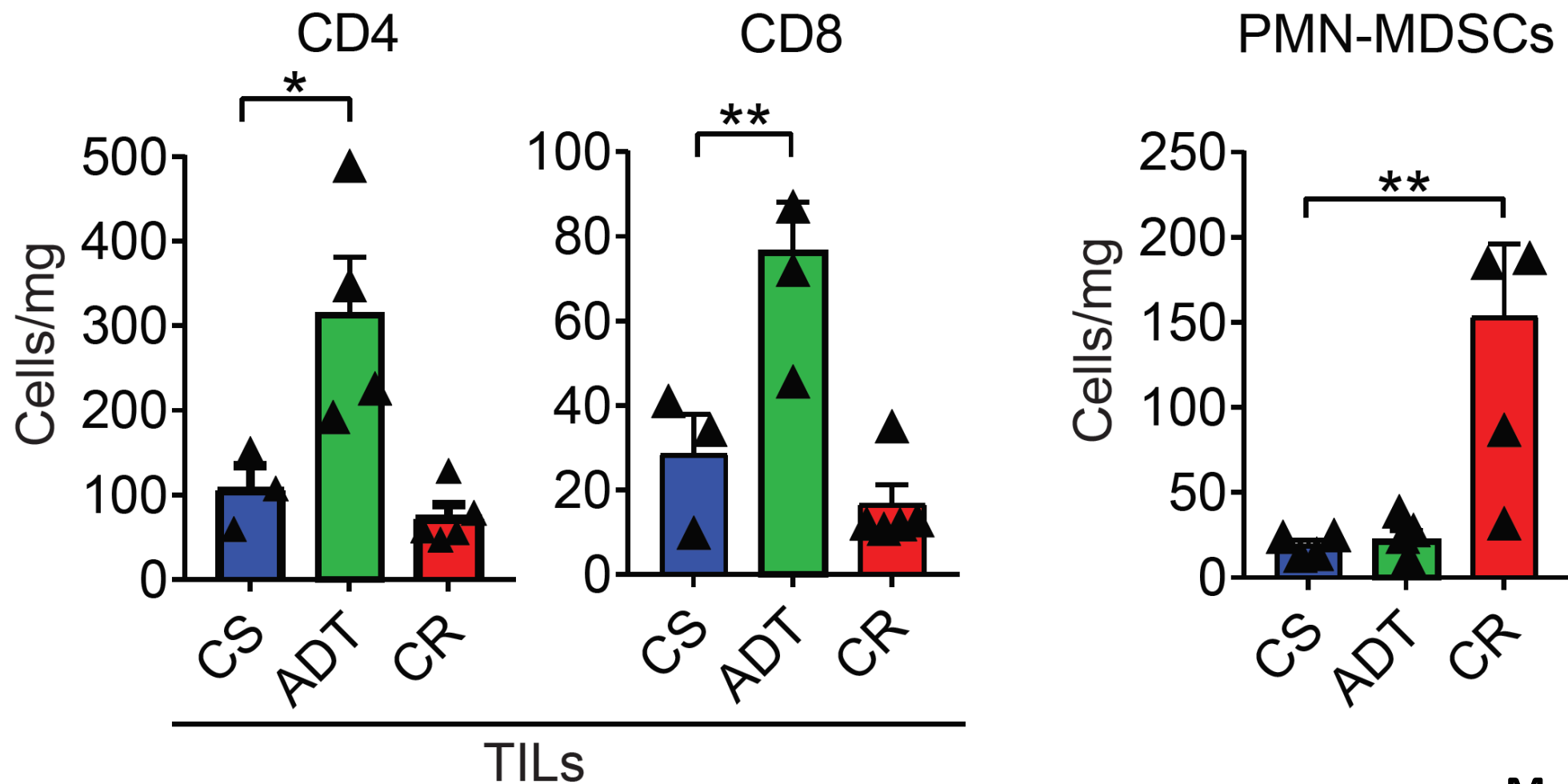
Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

IL-8 Expression is Increased in Human Prostate Cancer Epithelial Cells Following ADT



Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

Tumor Infiltrating PMN-MDSC Increase at The Time of CR

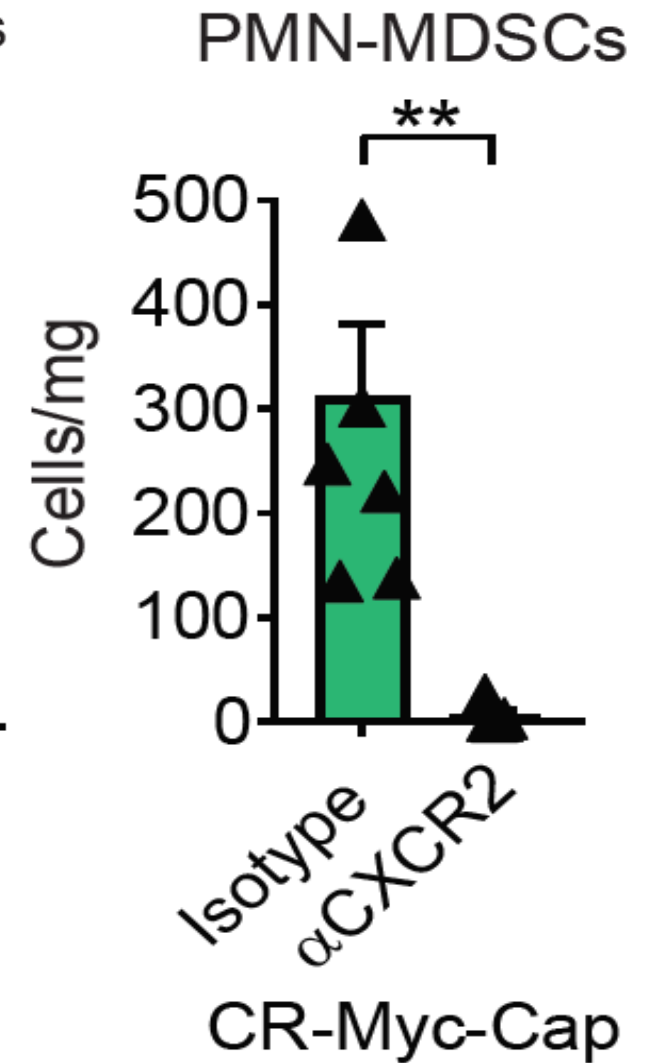
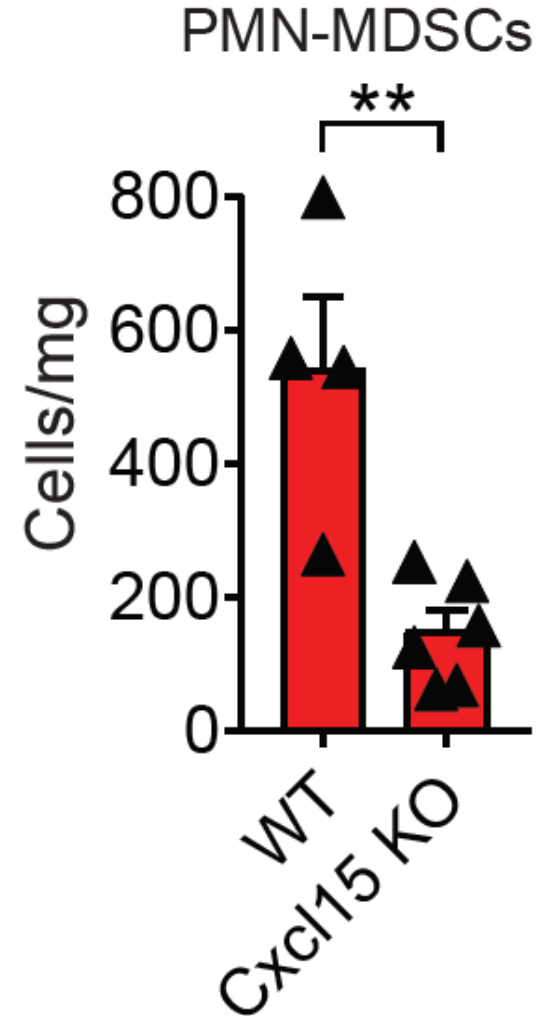
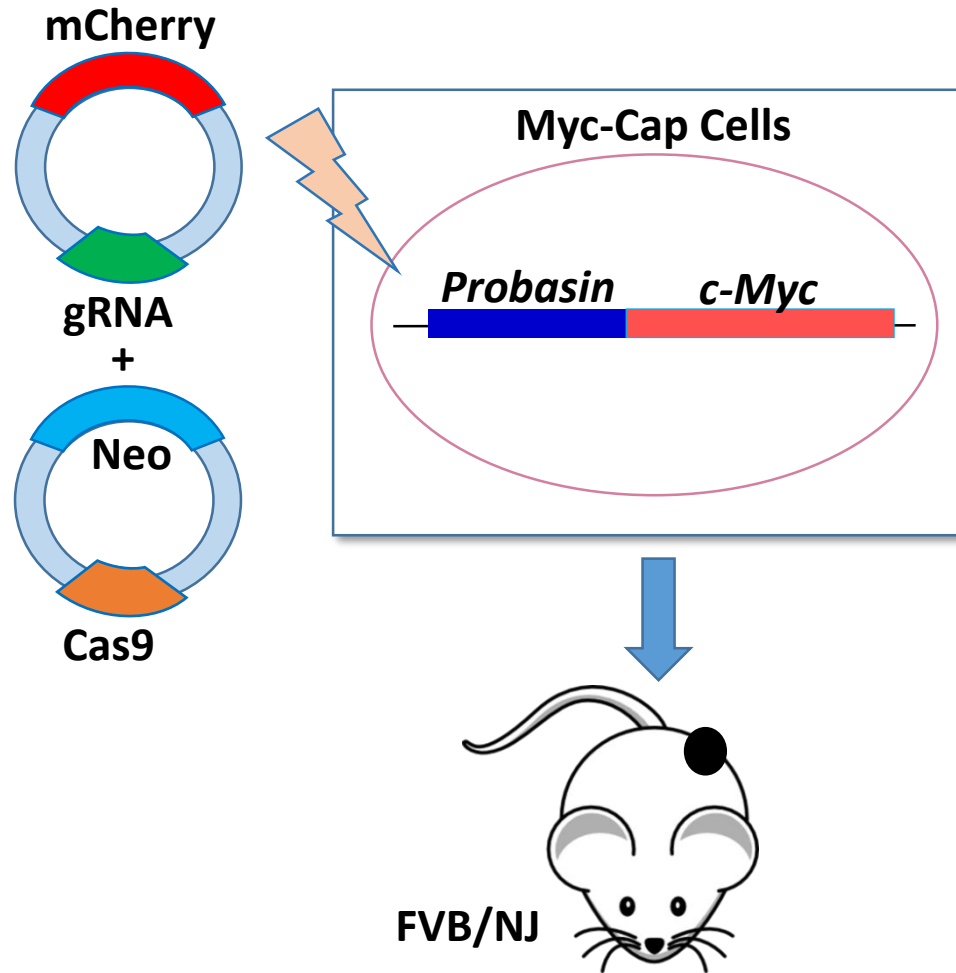


Myc-Cap Tumors

Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

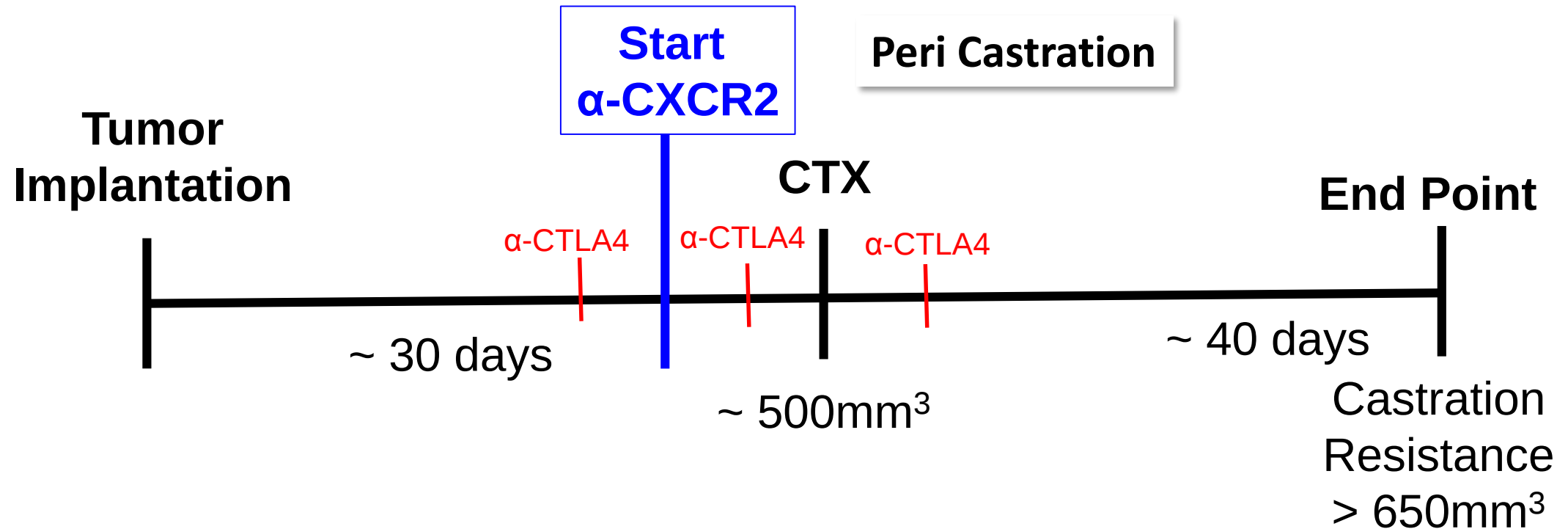
Tumor-Cell Derived Cxcl15 (mIL8) Drives PMN-MDSCs Recruitment in Mouse Tumors

CRISPR mIL-8 KO Mouse Cell Line



Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

What is the Effect of Combining CXCR2 and CTLA-4 Blockade?

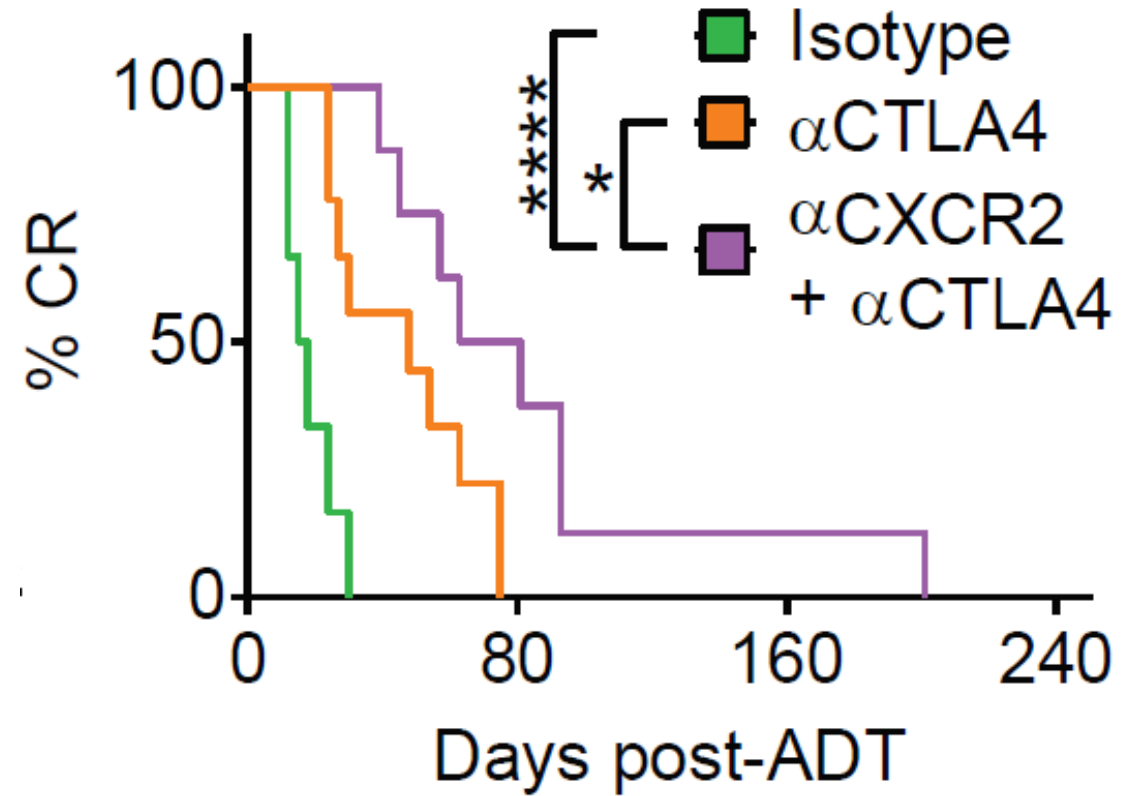
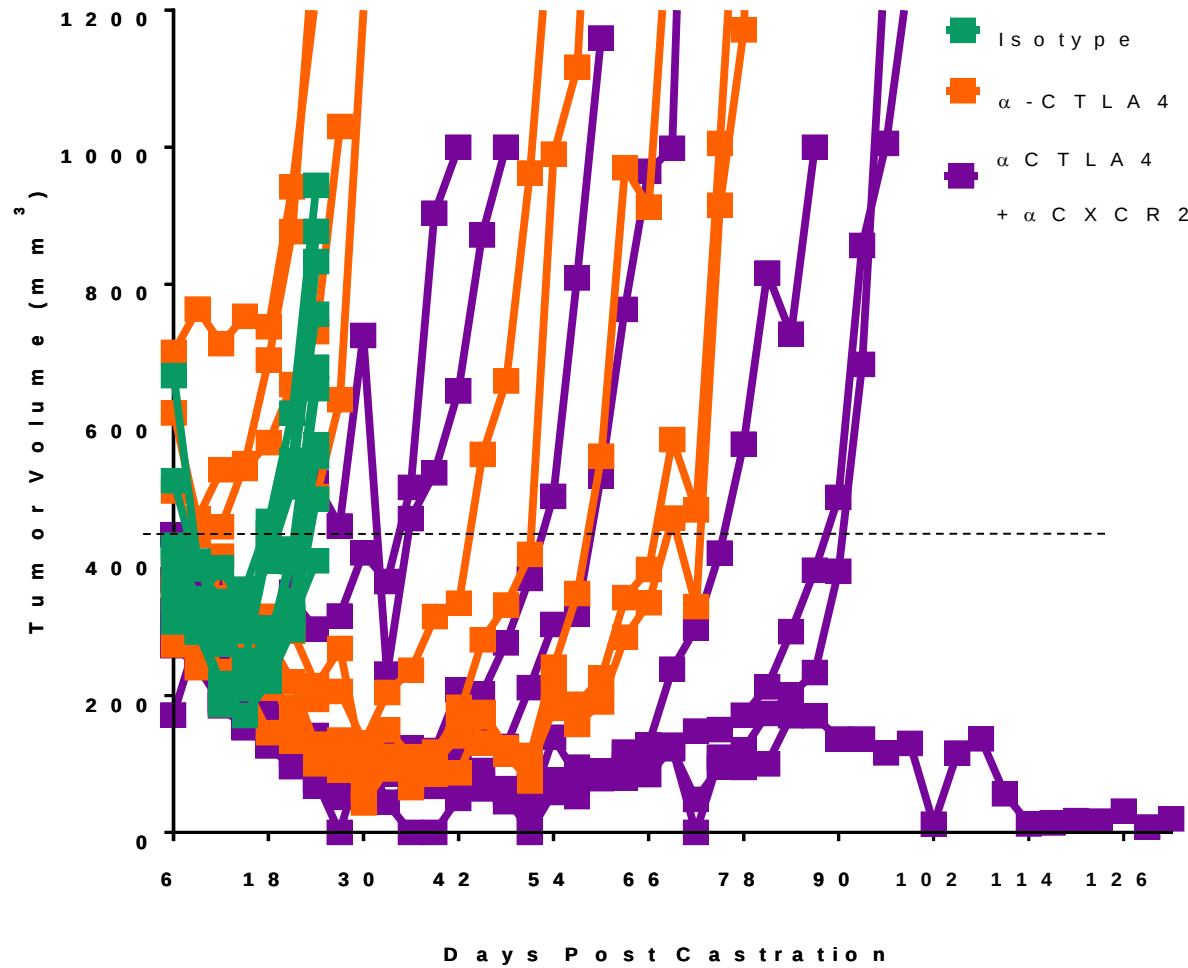


PMN Blockade: 3 doses of α -CXCR2 every 4 days

Inhibitory Pathway Blockade: 3 doses of α -CTLA4 every 3 days

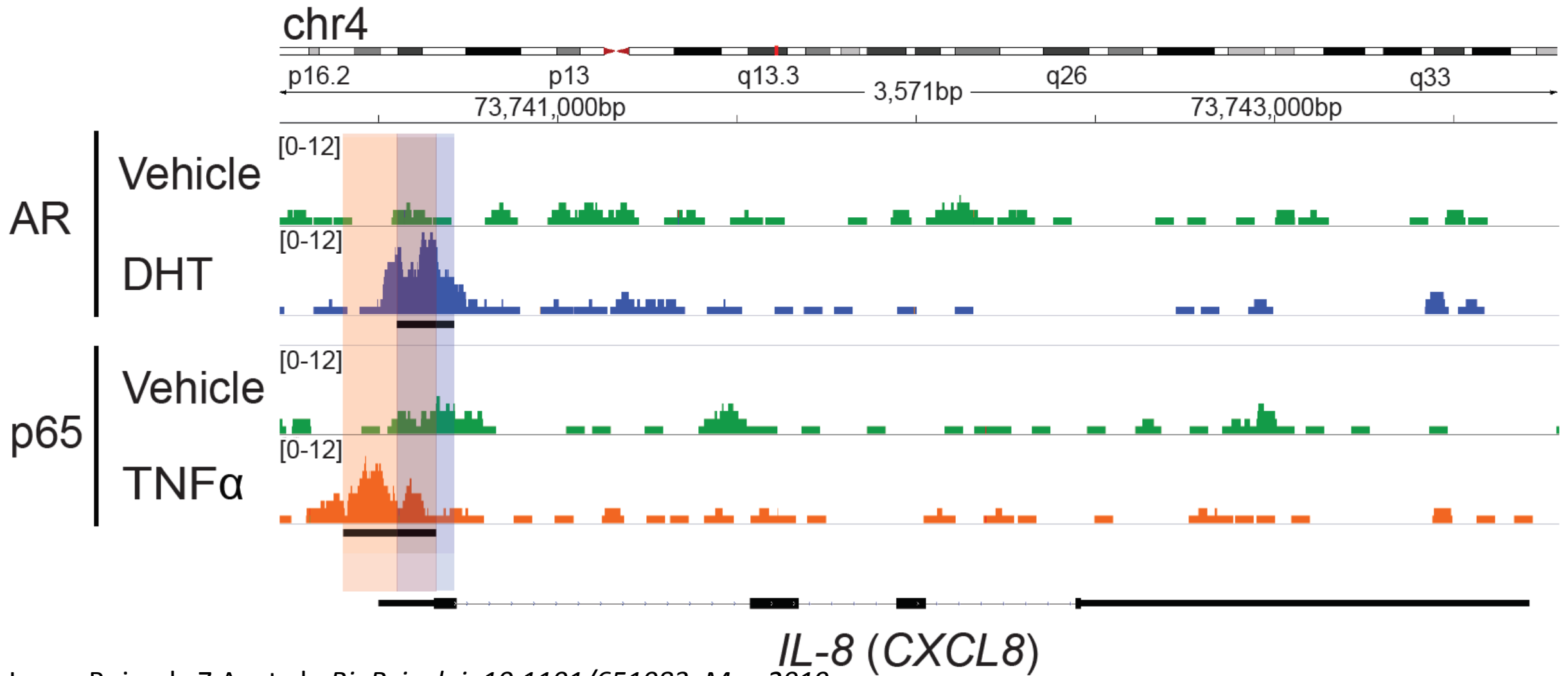
Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

CXCR2 Blockade Delays Tumor Progression of Established Mouse Tumors



Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

AR and NFκβ-p65 Bind to the *IL-8* Promoter



Lopez Bujanda Z.A. et al., *BioRxiv* doi: 10.1101/651083, May 2019.

- **IL-8 is upregulated following ADT.**
- **Targeting the IL-8 / CXCR2 pathway hinders the recruitment of PMN-MDSCs to the TME.**
- **Targeting ADT-mediated PMN-MDSC recruitment may delay the onset of CRPC by preventing T cell suppression at the TME.**



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