

SITC 2019

Gaylord National Hotel
& Convention Center

Nov. 6-10

NATIONAL HARBOR, MARYLAND



Society for Immunotherapy of Cancer



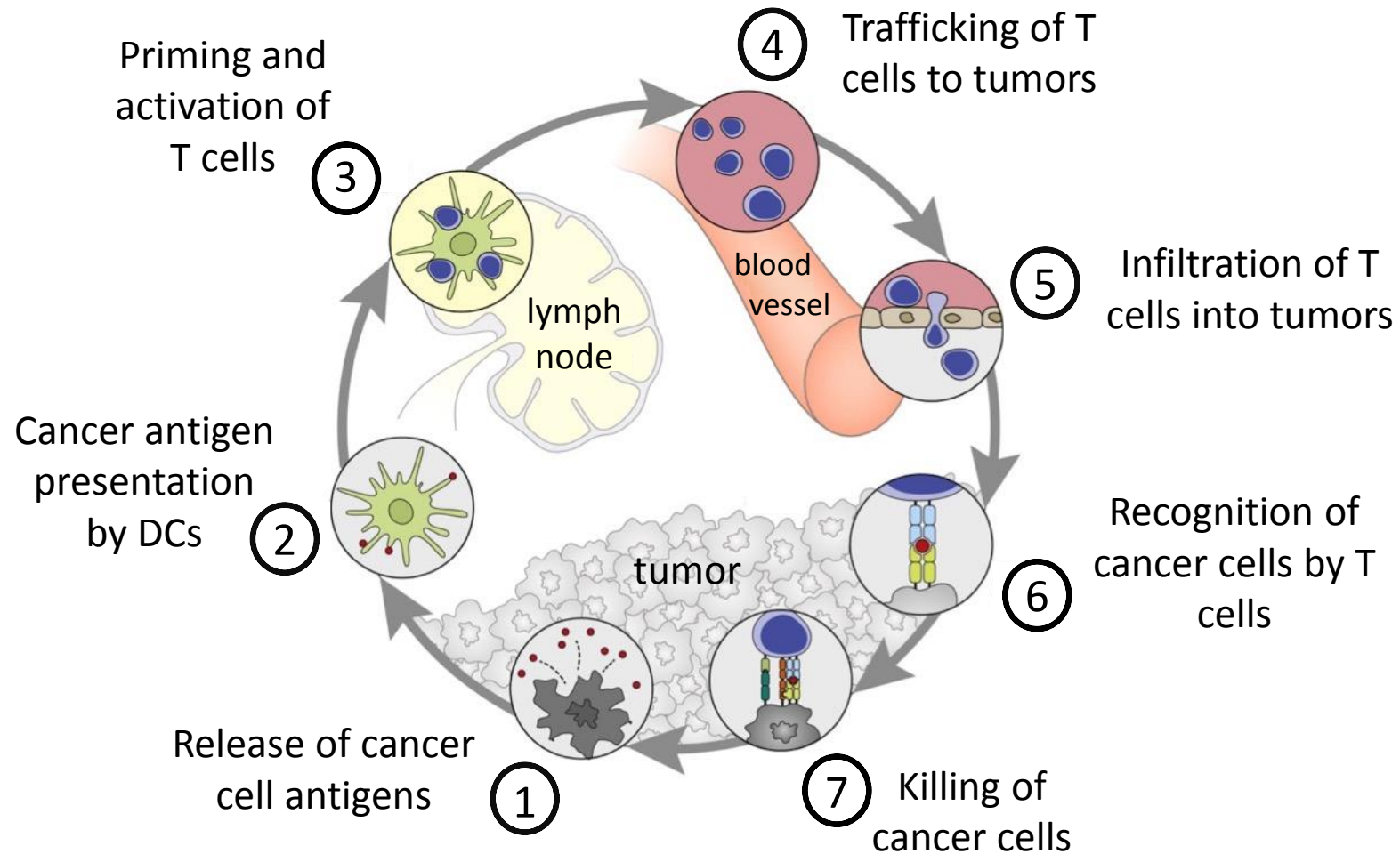
Single-dose immunotherapy that remodels the tumor microenvironment for subsequent curative responses to checkpoint blockade

Chensu Wang, Ph.D.

Darrell Irvine Laboratory

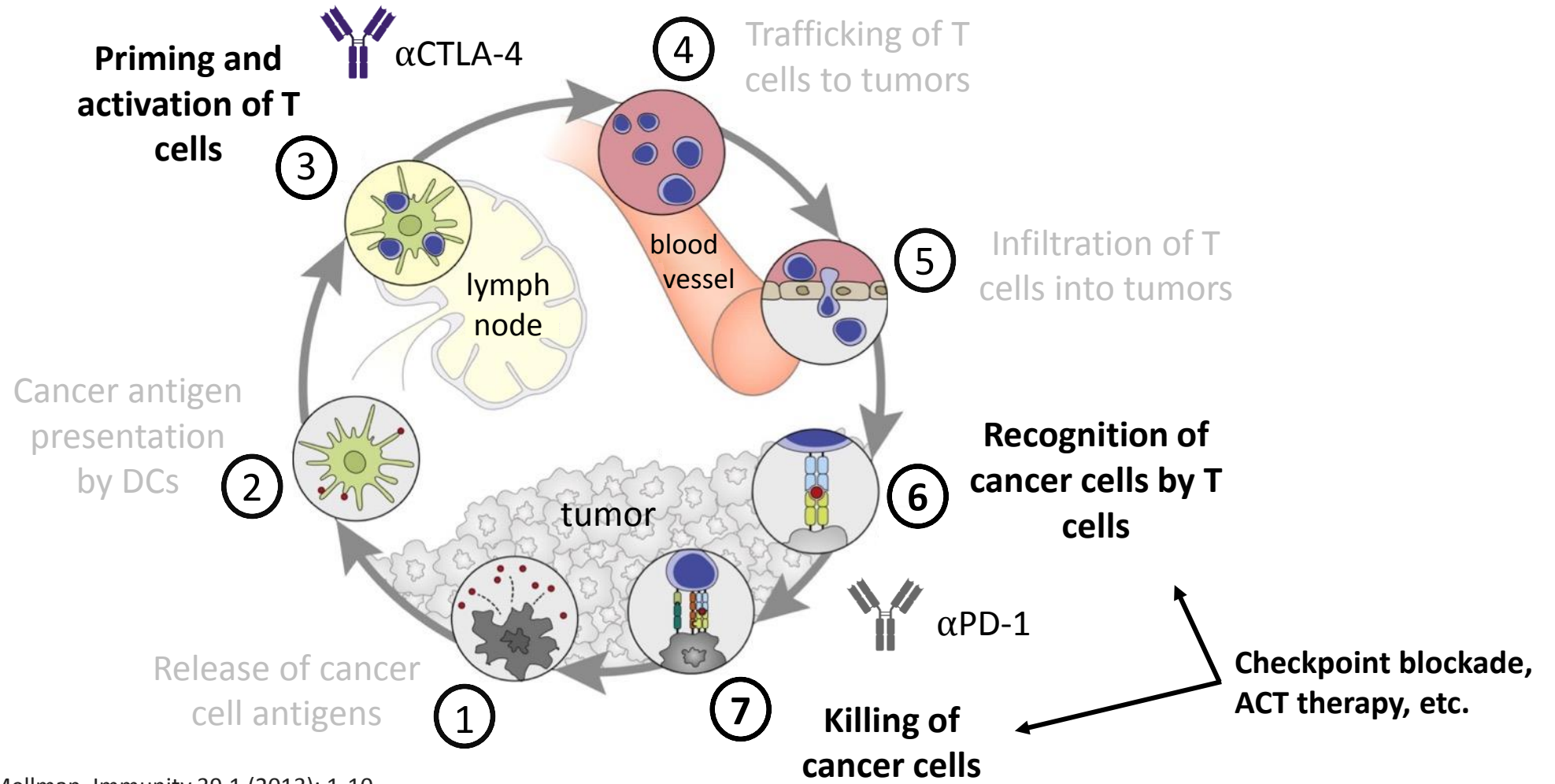
Koch Institute at MIT

The cancer-immunity cycle



Adapted from Chen, Daniel S., and Ira Mellman. Immunity 39.1 (2013): 1-10.

“Adaptive centric” immunotherapy armamentarium



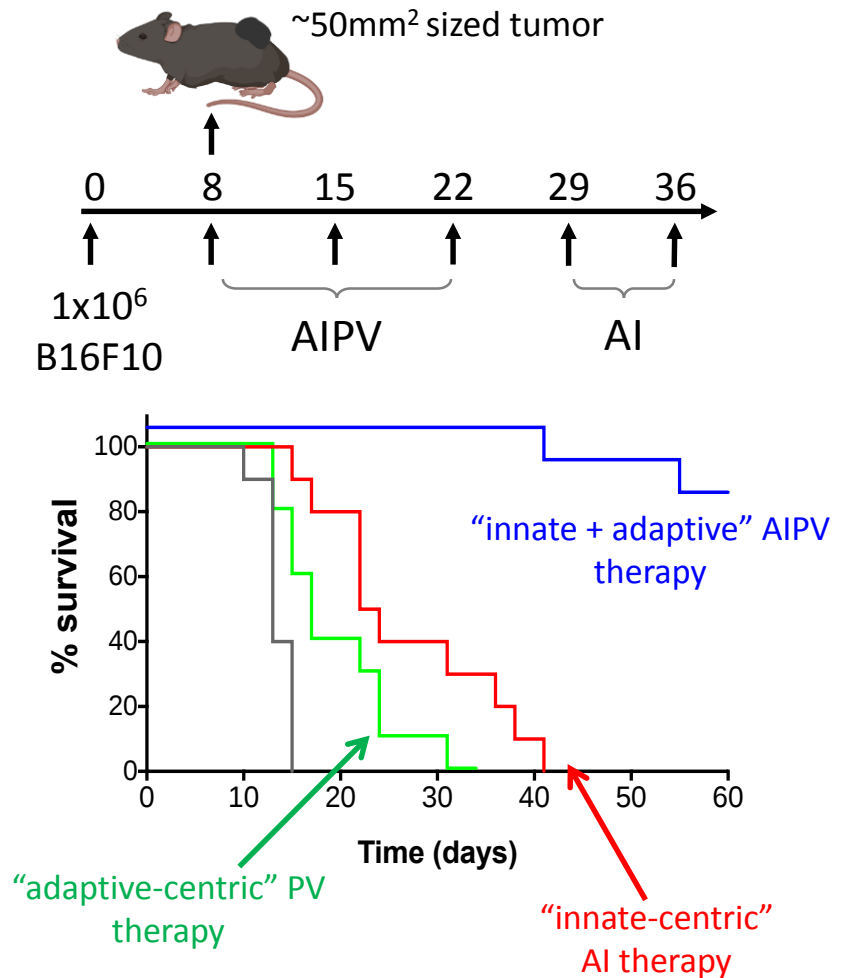
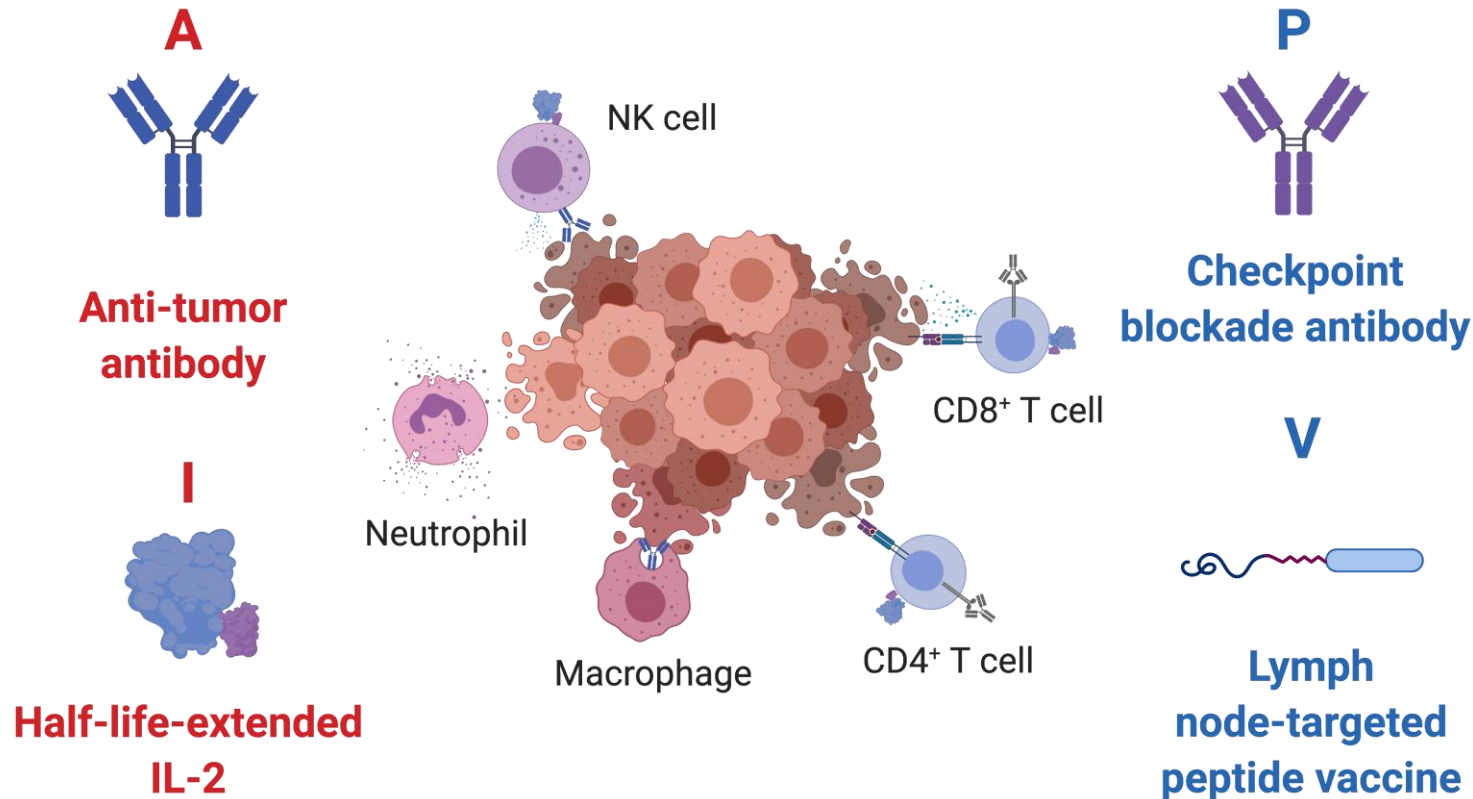
Adapted from Chen, Daniel S., and Ira Mellman. Immunity 39.1 (2013): 1-10.

Exploring a combination therapy aimed at recruiting combined innate and adaptive immune attack

Innate centric

"AIPV" therapy

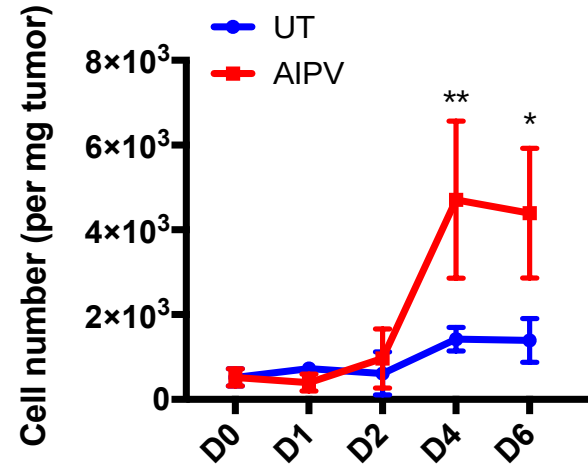
Adaptive centric



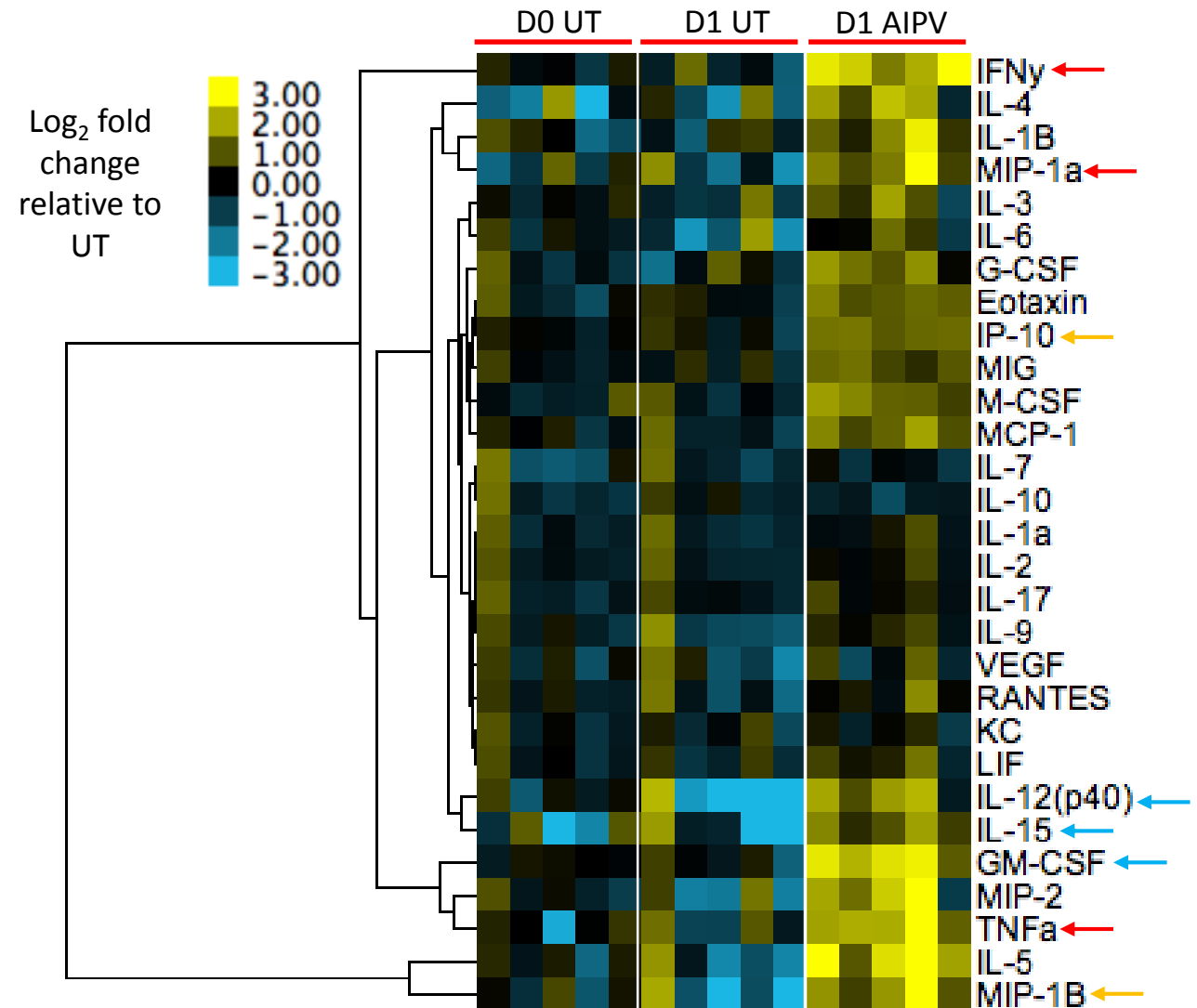
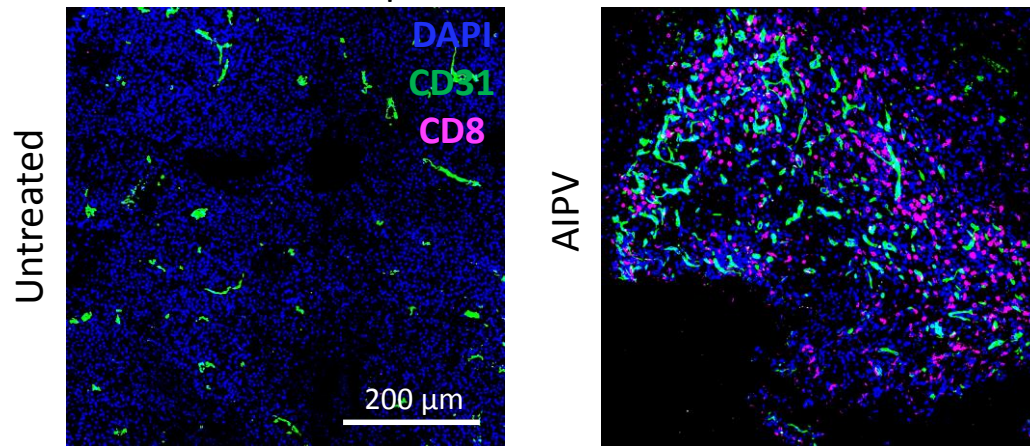
Moynihan, K. D., et al. (2016). *Nature Medicine* 22, 1402–1410

AIPV therapy rapidly remodels tumor microenvironment

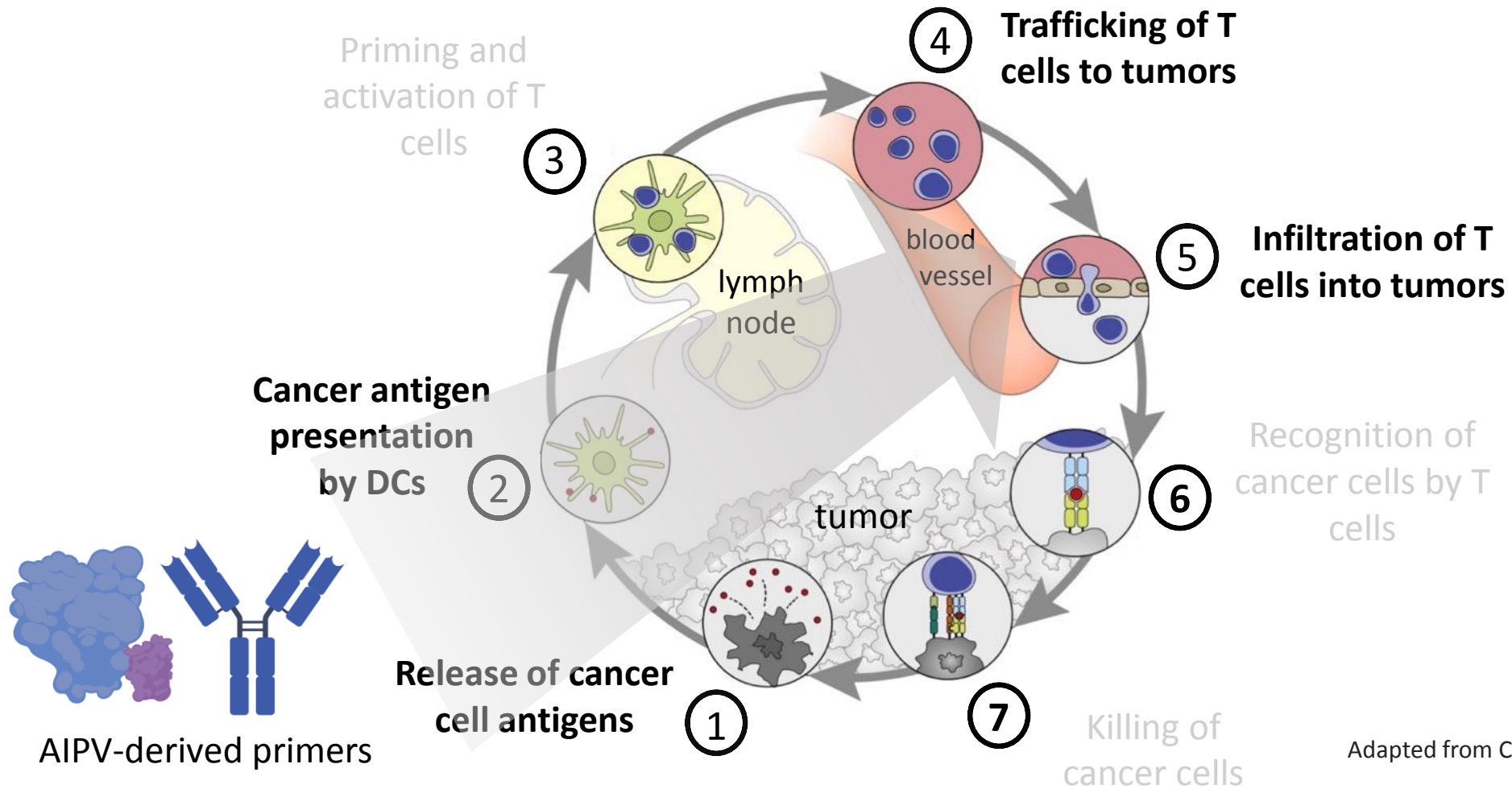
CD8⁺ T cell infiltration within a week of treatment



B16F10 tumor; 6d post first dose of AIPV:

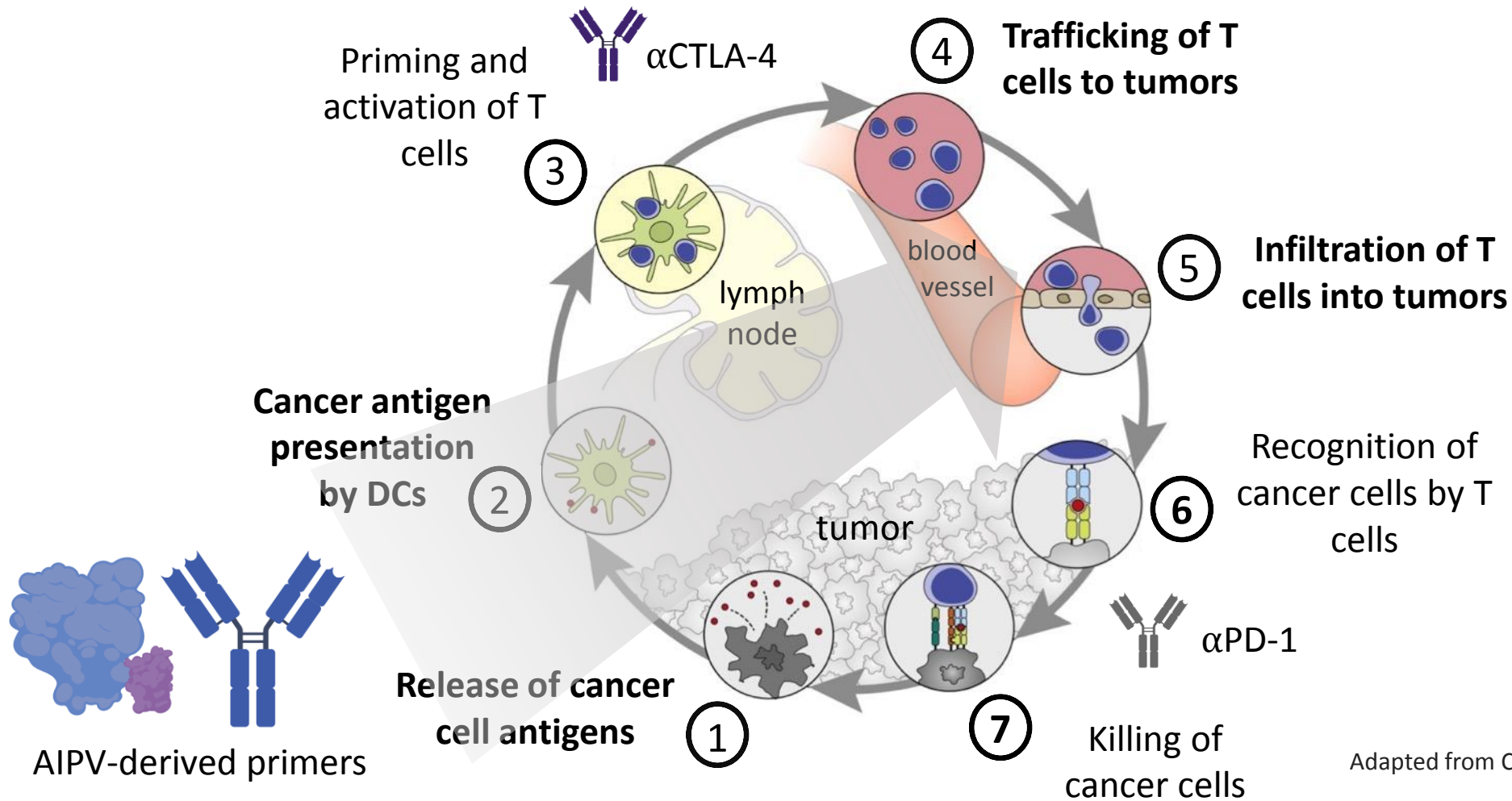


Could we simplify AIPV as a priming strategy that improves responsiveness to approved checkpoint blockade therapy?



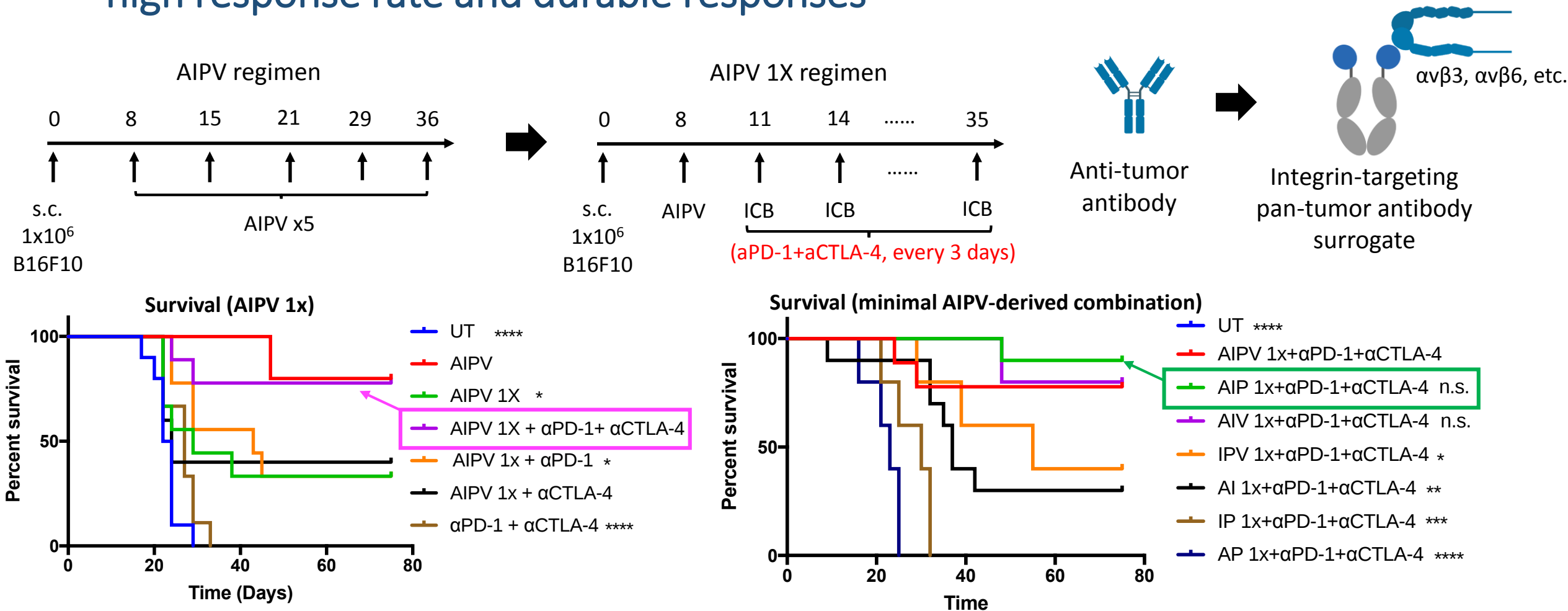
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Could we simplify AIPV as a priming strategy that improves responsiveness to approved checkpoint blockade therapy?



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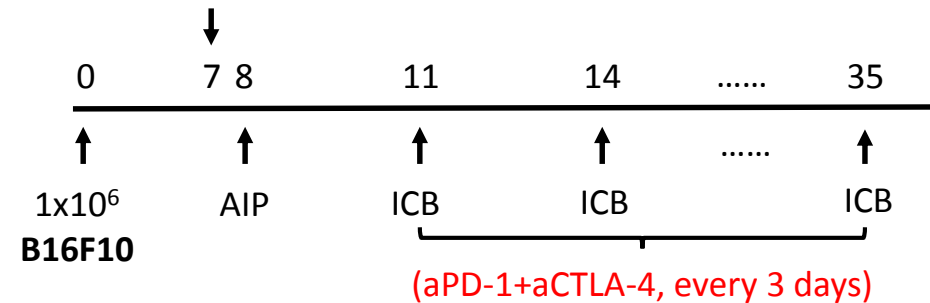
Single-dose AIP combined with immune checkpoint blockades results in high response rate and durable responses



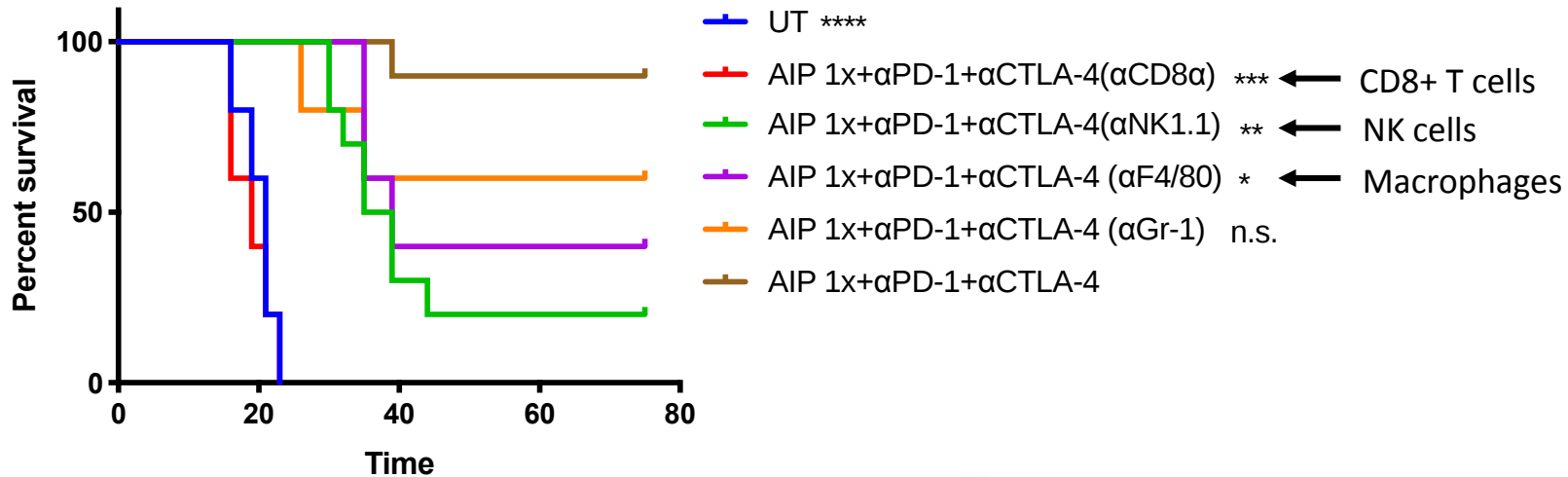
Kwan, Byron H., et al. *J Exp Med* 214.6 (2017): 1679-1690;
Currier, Nicolas V., et al. *Mol. Cancer Ther.* 15.6 (2016): 1291-1300.

Efficacy is dependent upon both innate and adaptive immunity

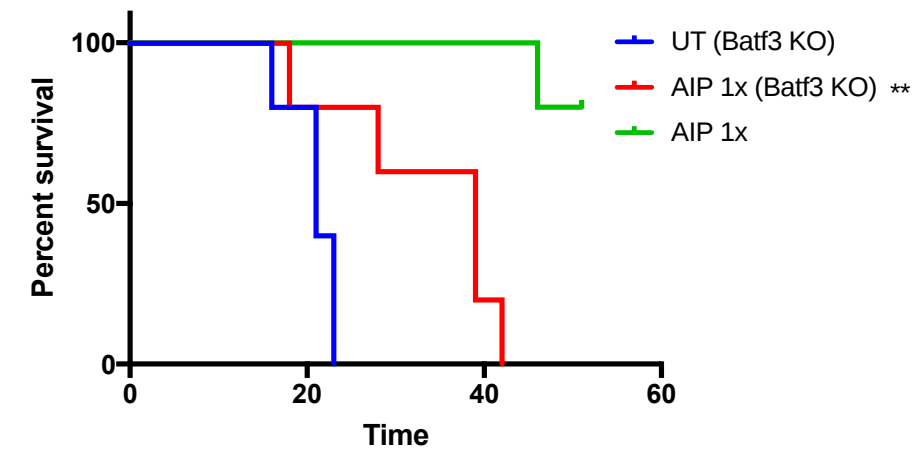
Neutralizing Abs, 2-3 times/week



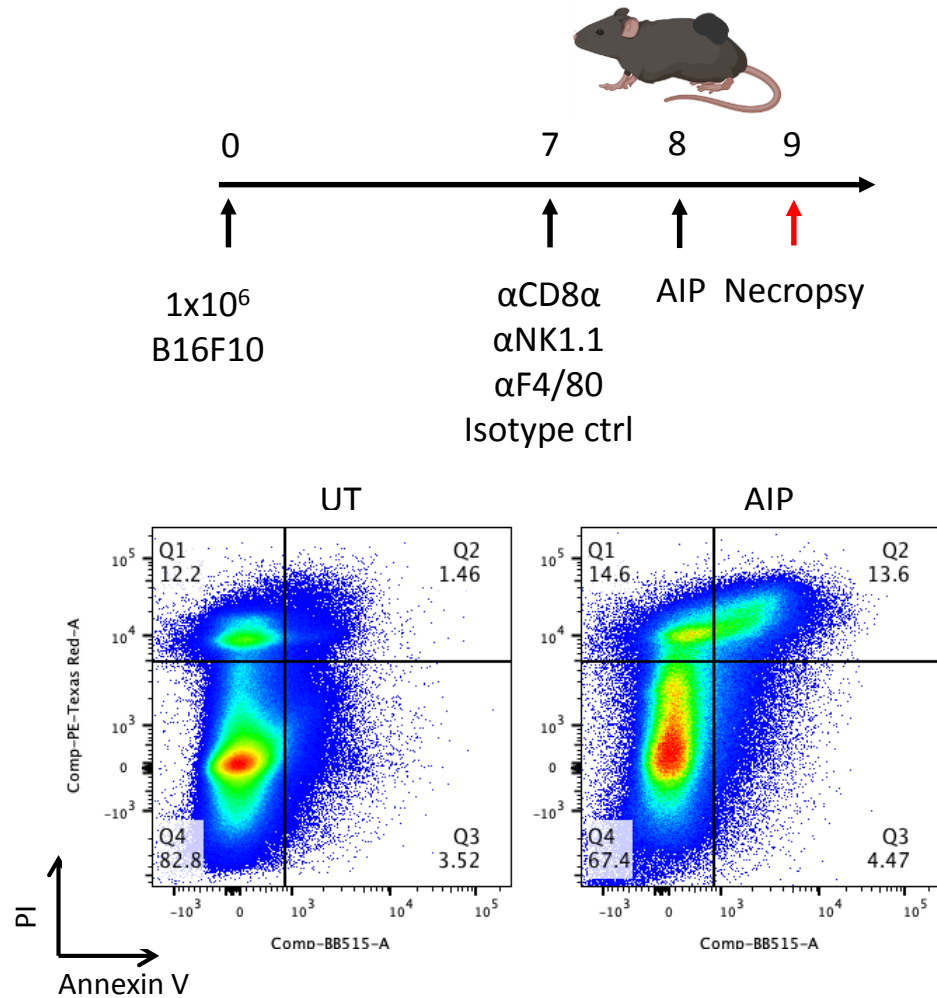
Survival (WT C57BL/6)



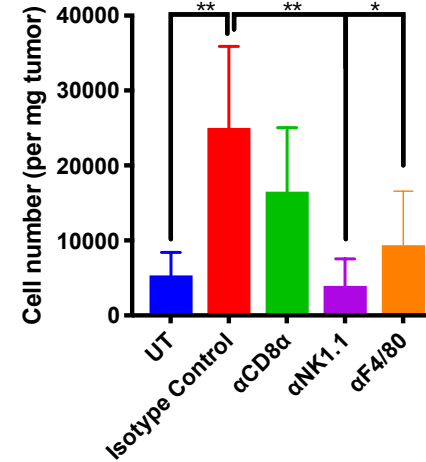
Survival (Batf3 KO model)



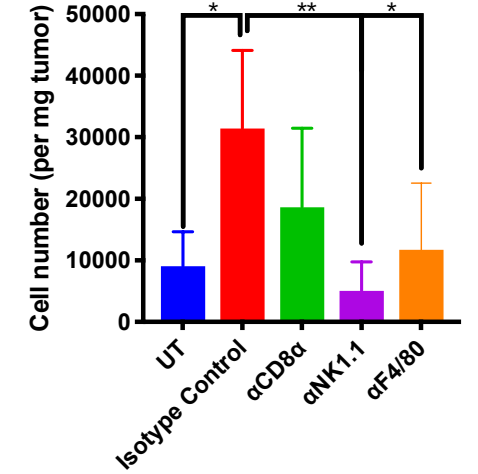
NK cell- and macrophage-dependent initial tumor killing



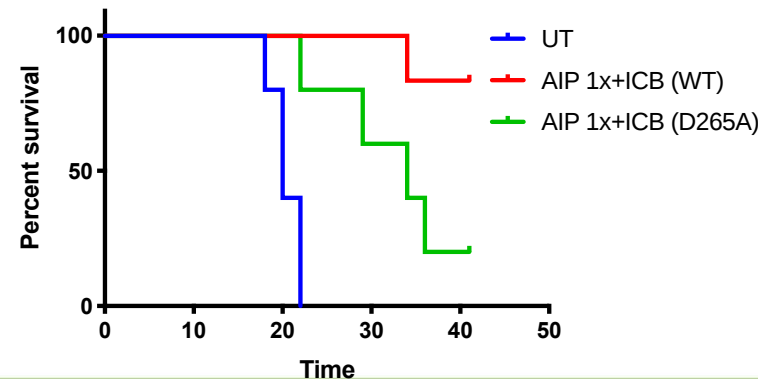
Apoptotic cell death (Annexin V+, PI+)



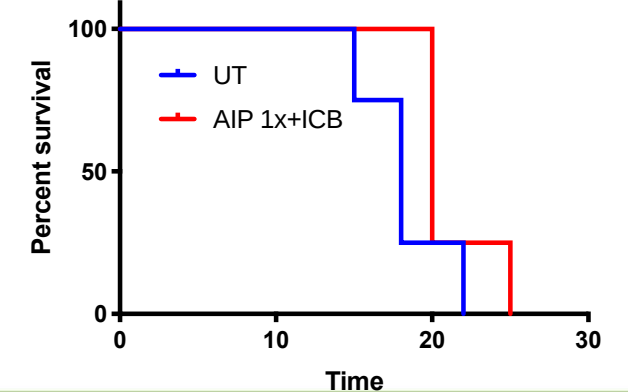
Immunogenic cell death (Calreticulin+)



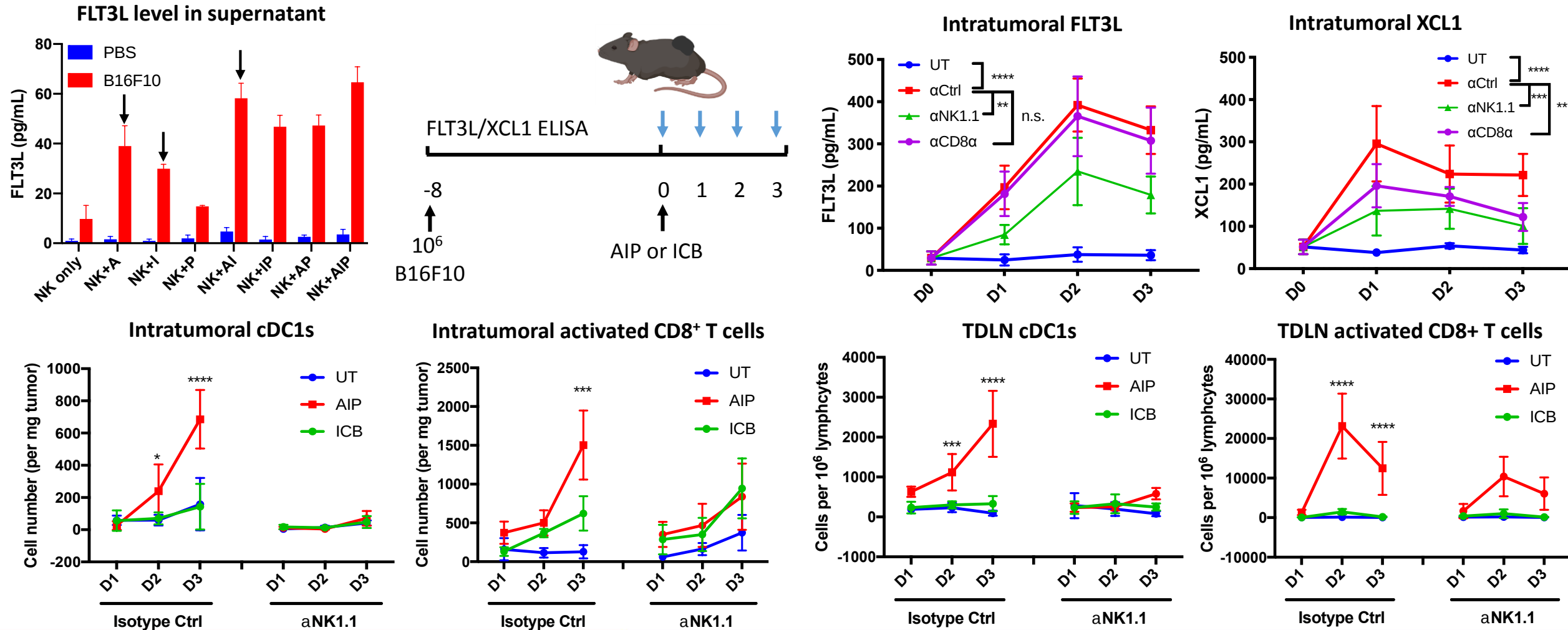
Survival (Fc effector function efficiency)



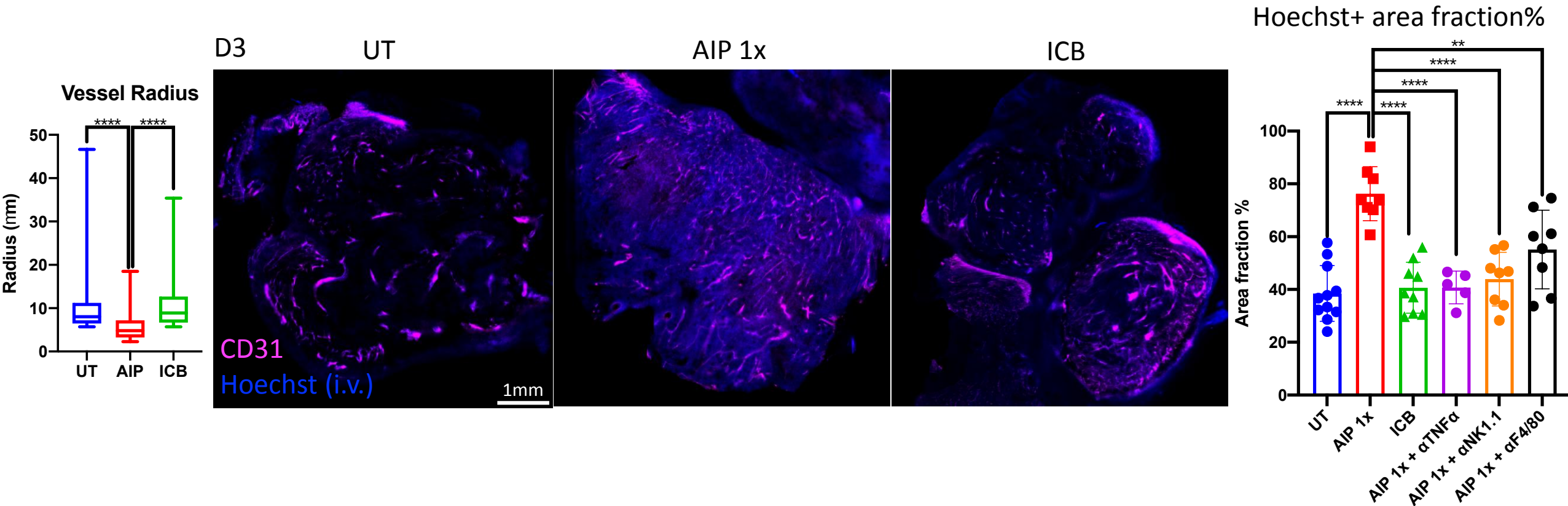
Survival (Fcgr3 KO model)



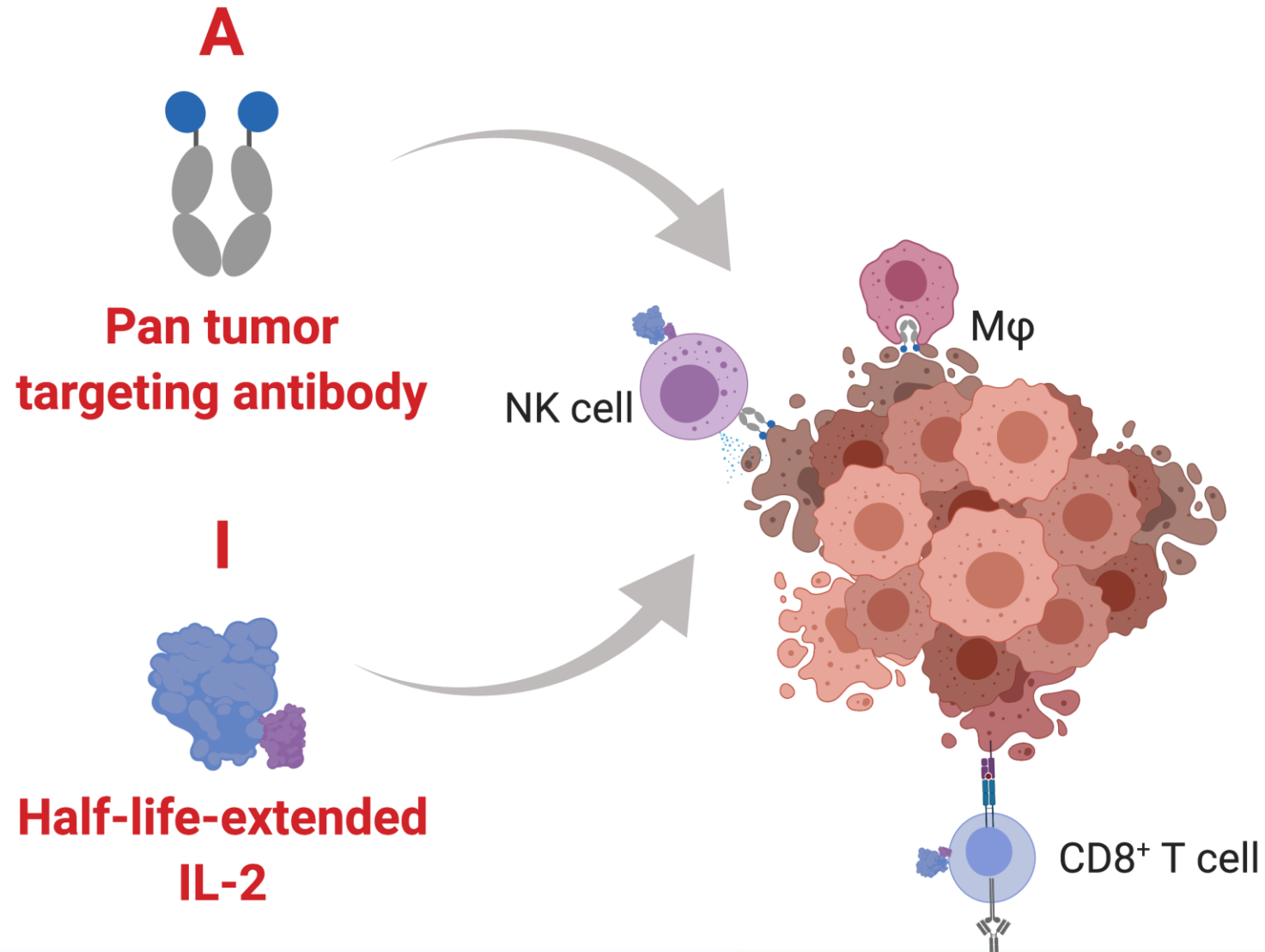
NK cells attract and maintain cDC1s and promote CTL-mediated cancer immunity control in TME



AIP induces vascular normalization likely through NK cell- and macrophage-secreted TNF α



Innate Immunity



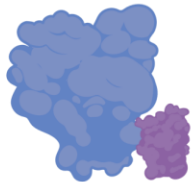
Innate Immunity

A

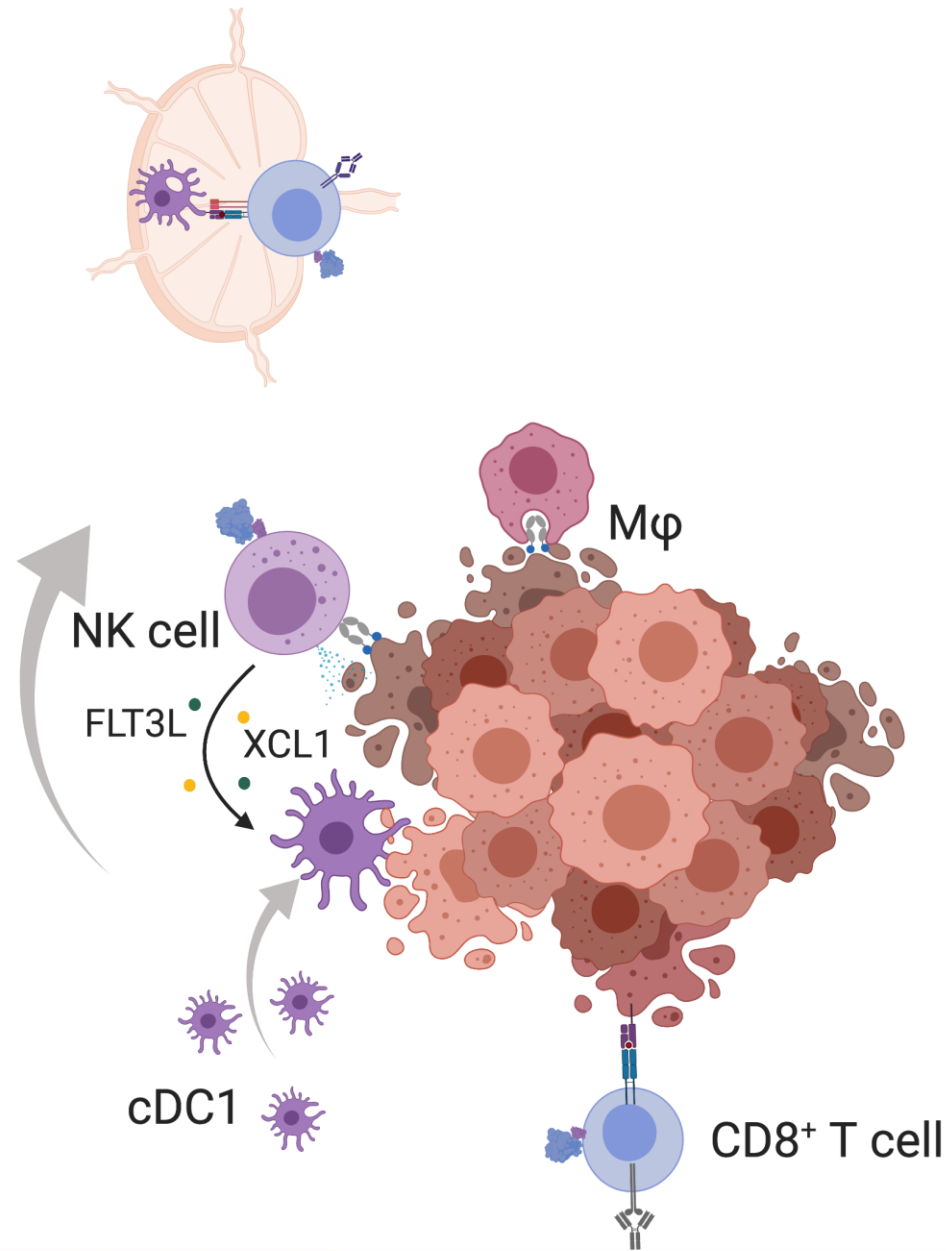


Pan tumor targeting antibody

1



Half-life-extended IL-2



Innate Immunity

A

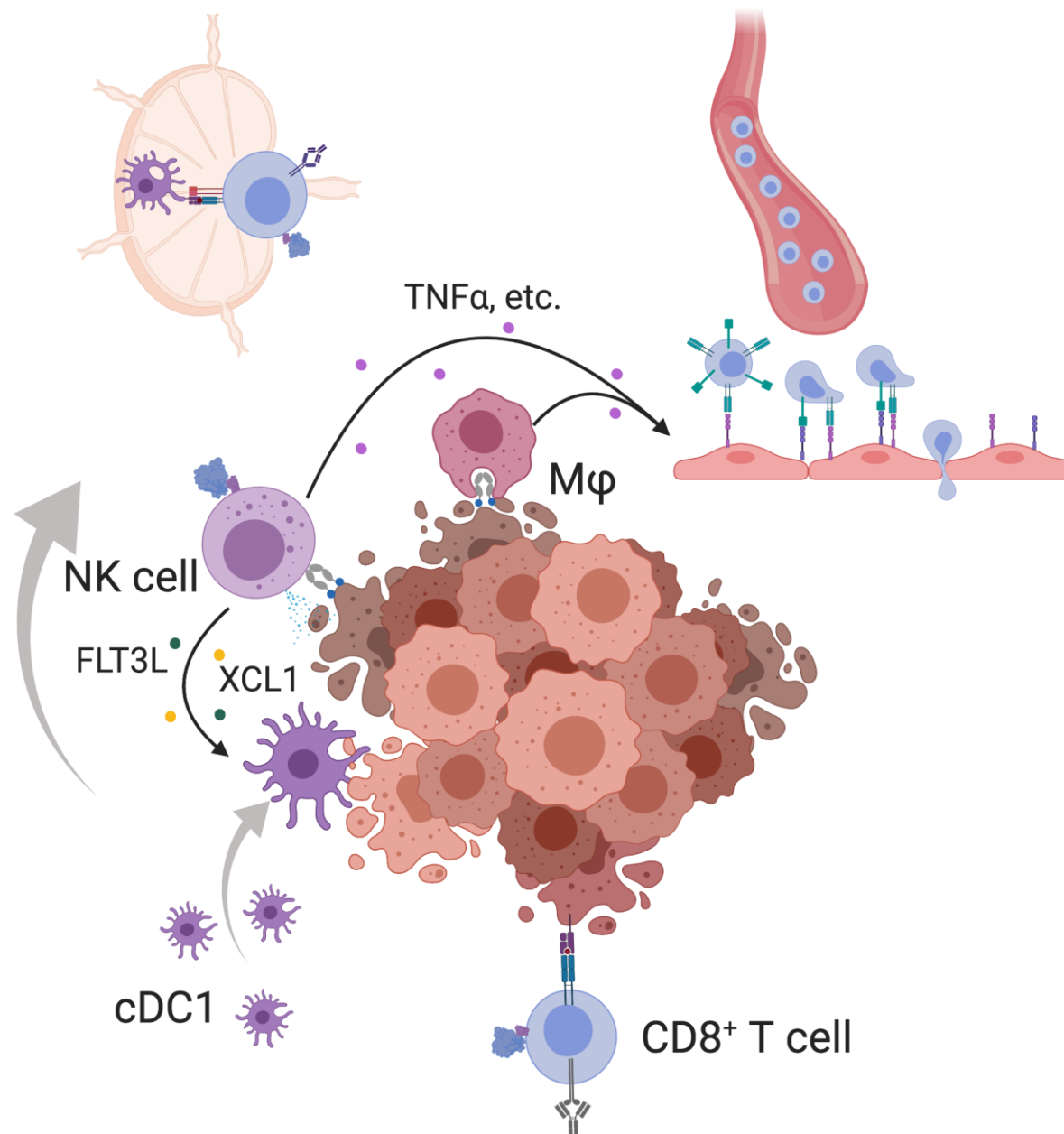


**Pan tumor
targeting antibody**

I



**Half-life-extended
IL-2**



Innate Immunity

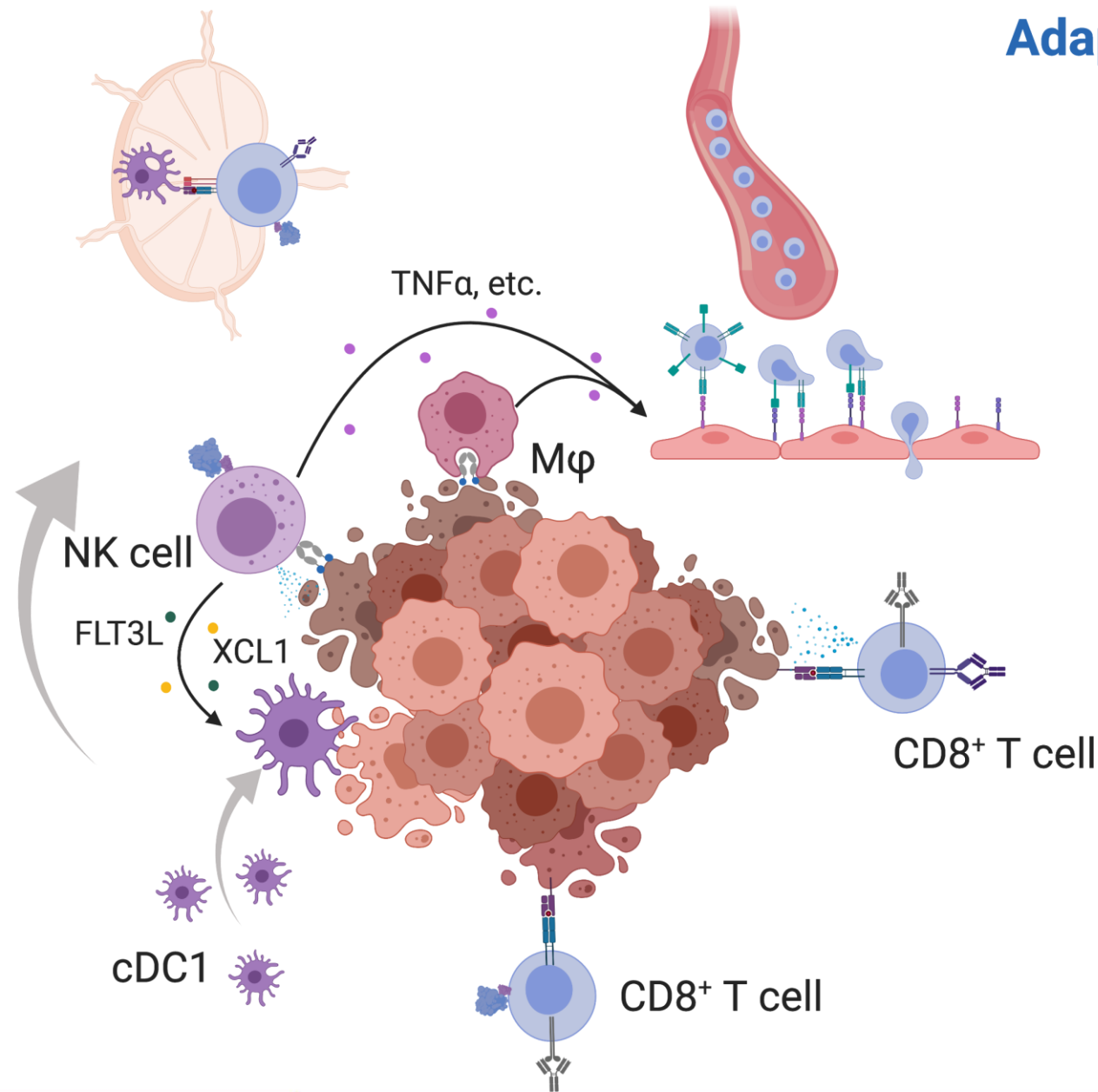
Adaptive Responses

A

**Pan tumor
targeting antibody**

I

**Half-life-extended
IL-2**



ICB

**Checkpoint
blockade
antibody**

Irvine Lab+Alumni

Darrell Irvine

Ayush Thomas
Maurice Bukenya
Aereas Aung
Simon Liang
Jack Martin
Jason Chang
Heikyung Suh
Kelly Moynihan
Coralie Backlund
Kavya Rakhra
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