



# Potentialiation of T-cell mediated tumor killing via modulation of the fas/fasL pathway

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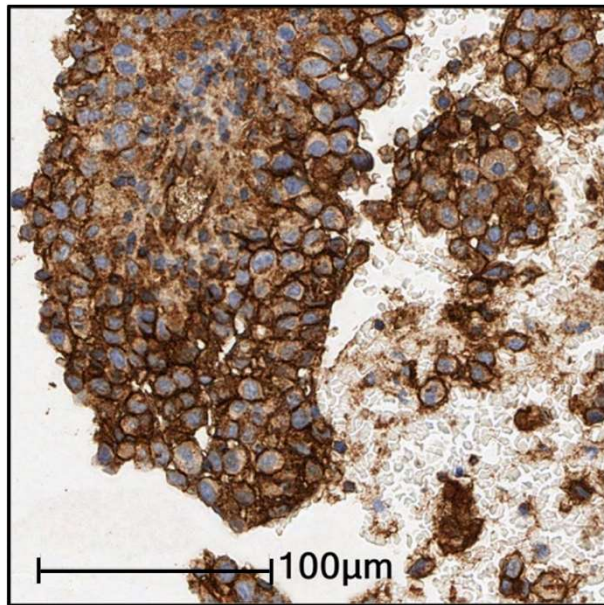
Society for Immunotherapy of Cancer

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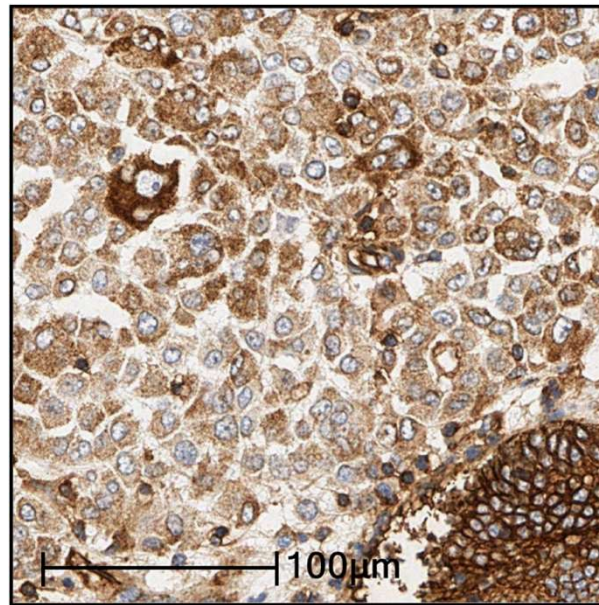
# Disclosures

I have no financial disclosure or conflicts of interest with the material in this presentation.

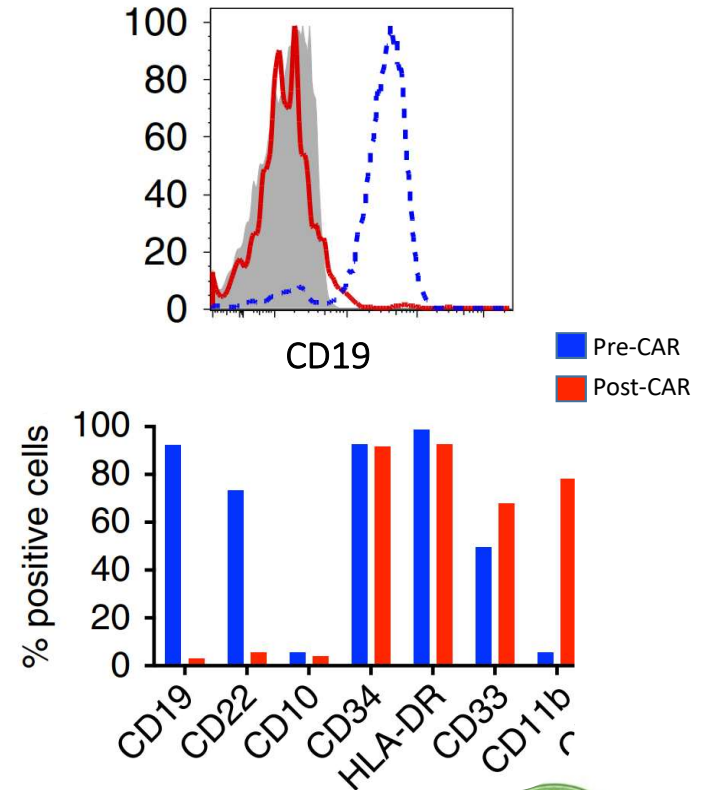
# Antigen escape is common method of immune evasion



**MHC I (Pre-Anti-PD1)**



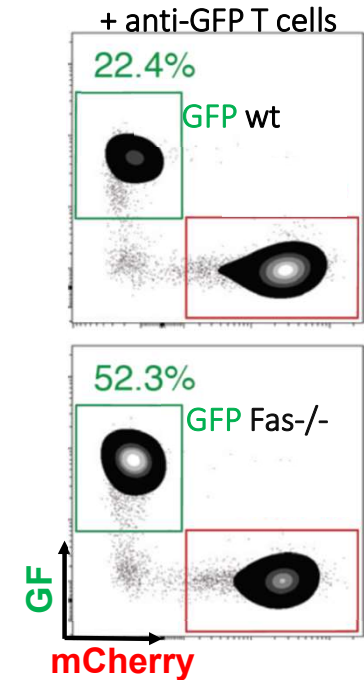
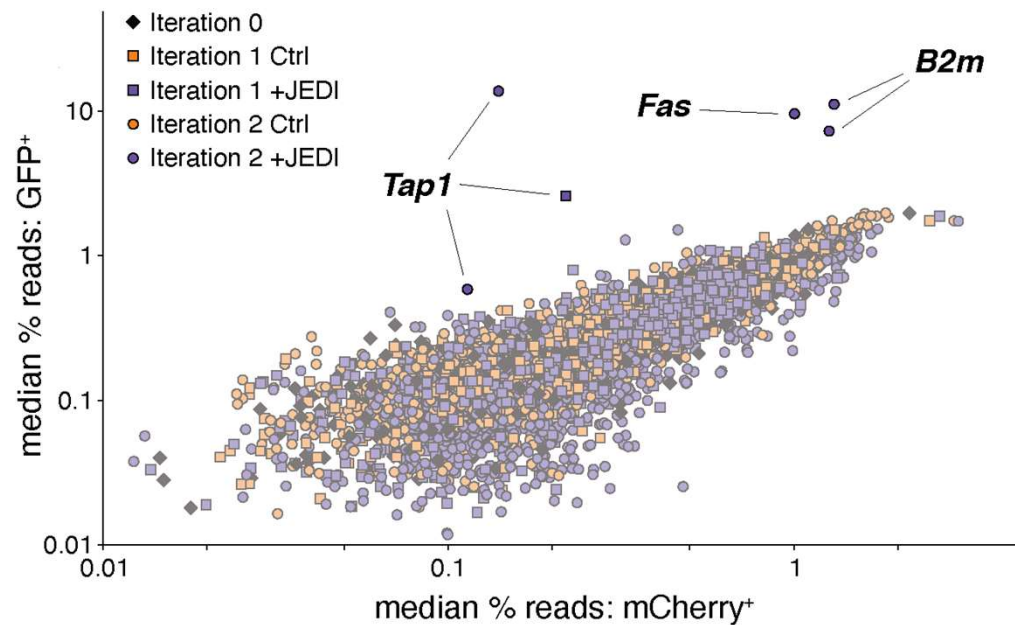
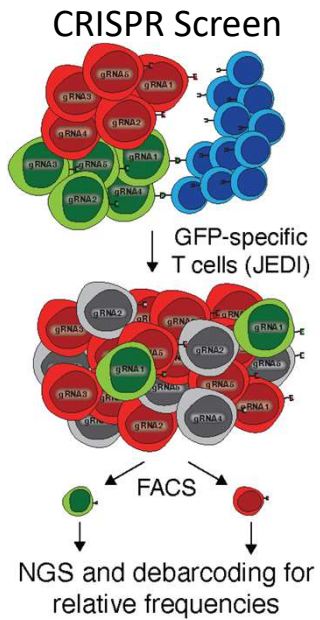
**MHC I (Relapse)**



Zaretsky et al, NEJM 2016

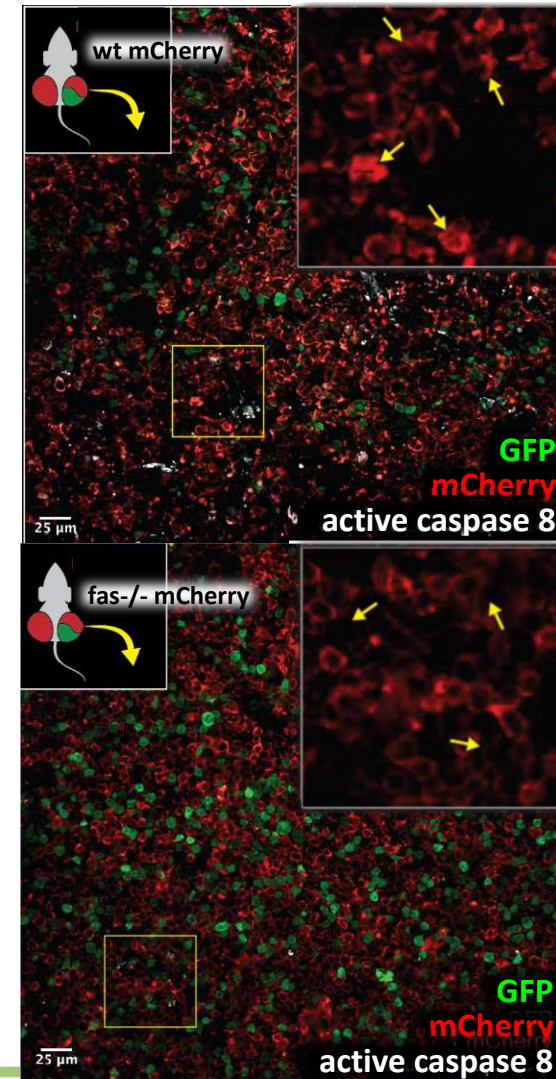
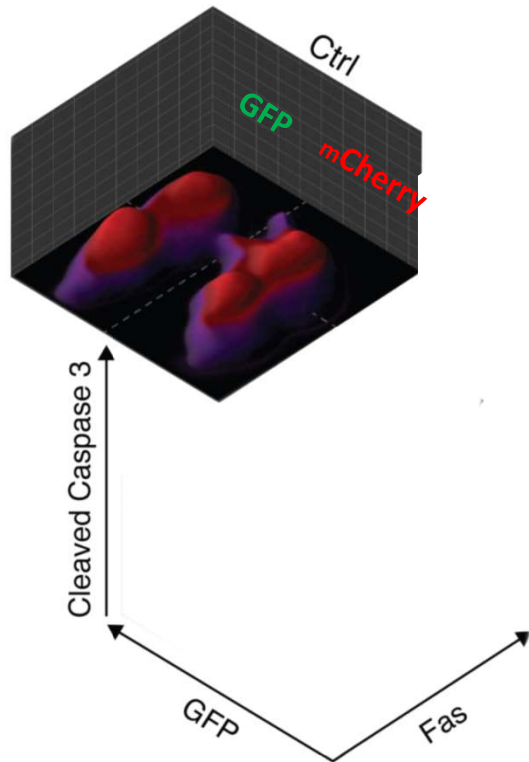
Jacoby E et al., *Nat Commun.* 2016

# Fas is a critical T-cell effector molecule





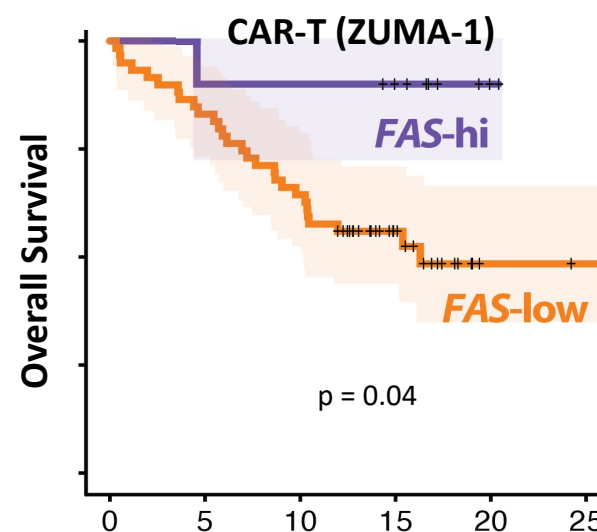
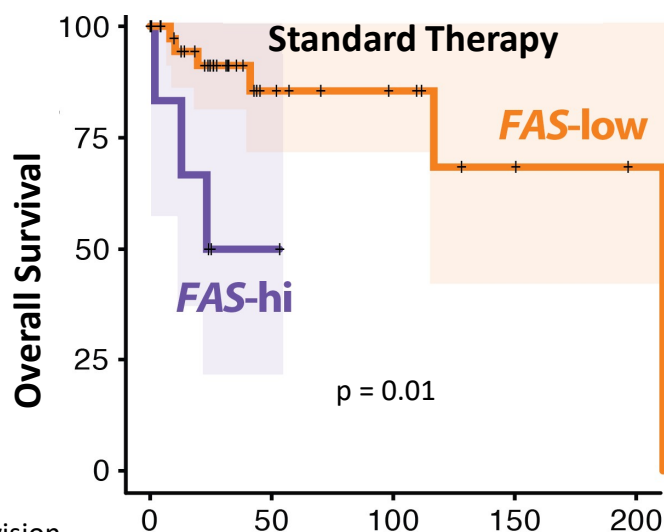
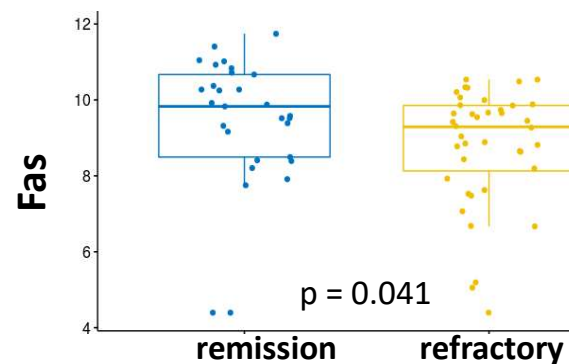
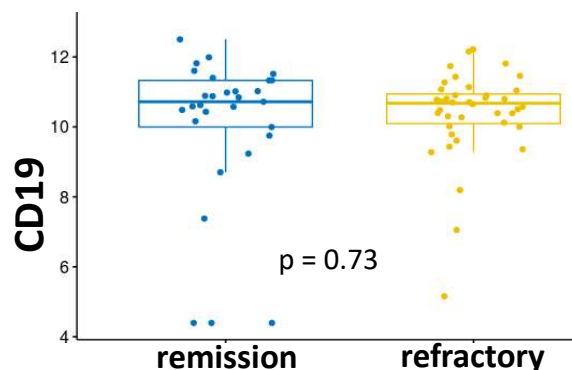
# Fas mediates **bystander** killing *in vitro* and *in vivo*



Upadhyay R, et al., In Revision



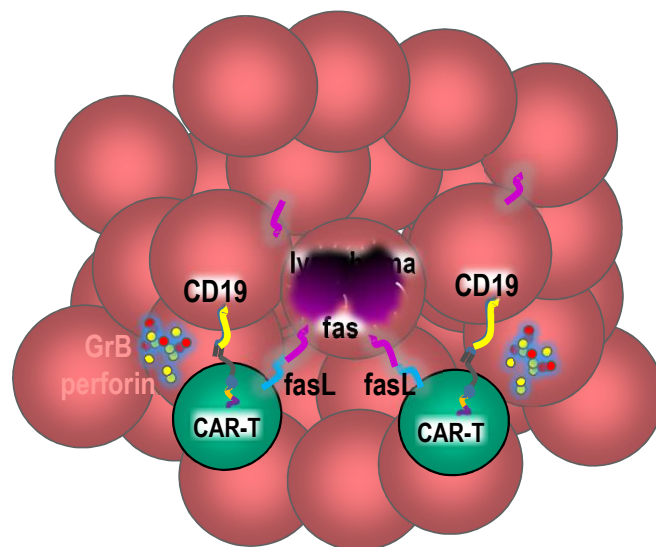
# Fas predicts CAR-T patient's response and survival



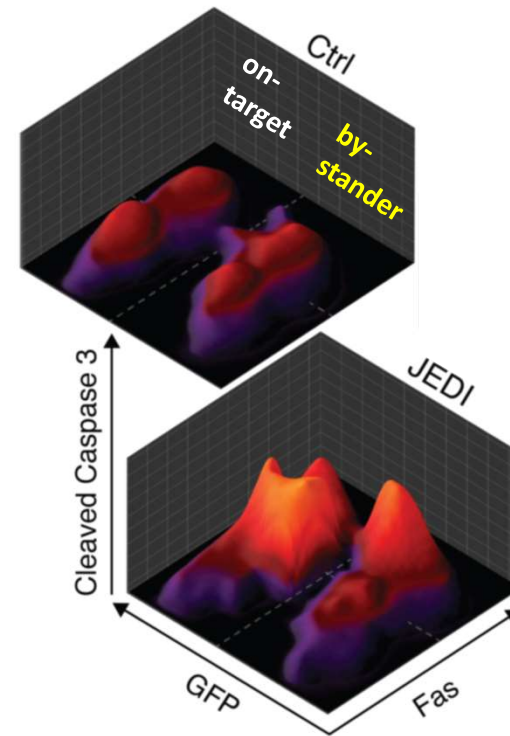
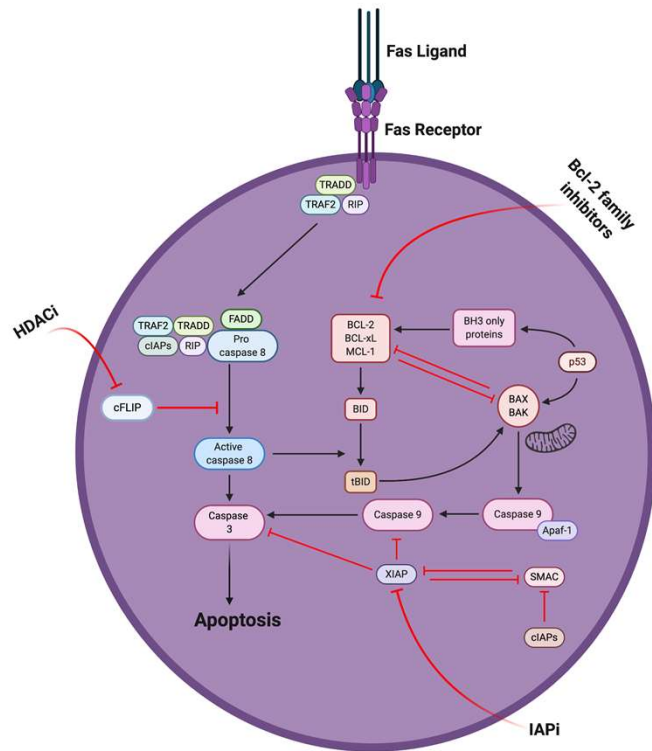
Upadhyay R, et al., In Revision

# Potentiate *bystander* tumor killing to prevent antigen escape

**Hypothesis:** increasing bystander killing will selectively eliminate Ag<sup>+</sup> tumor cells and prevent tumor relapse



# Modulating Fas signaling can increase on-target and bystander killing in vitro



Upadhyay R, et al., In Revision



## Conclusions:

- Bystander tumor cell killing *may* already be occurring in our patients receiving T-cell based therapies (CAR-T, bispecific mAb, checkpoint blockade).
- Bystander killing appears almost completely fas-mediated.
- On-target and bystander killing can be potentiated with fas modulators.
- Combining fas signaling modulators with T-cell therapies might prevent antigen escape and tumor relapse.



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