

Novel Approaches to Tumor Microenvironment Modulation for Enhanced Cancer Immunotherapy

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Disclosures

InnDura Therapeutics (co-founder & SAB)

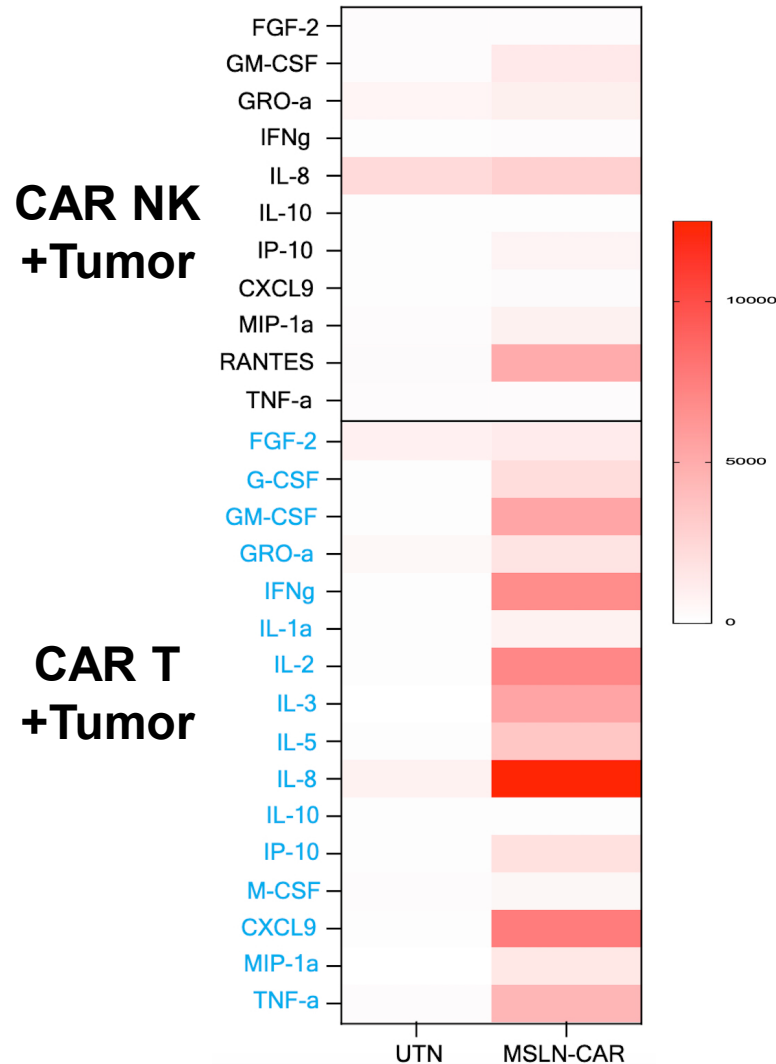
Parker Institute for Cancer Immunotherapy (member/funding)

Glycostem (SAB, paid consultant)

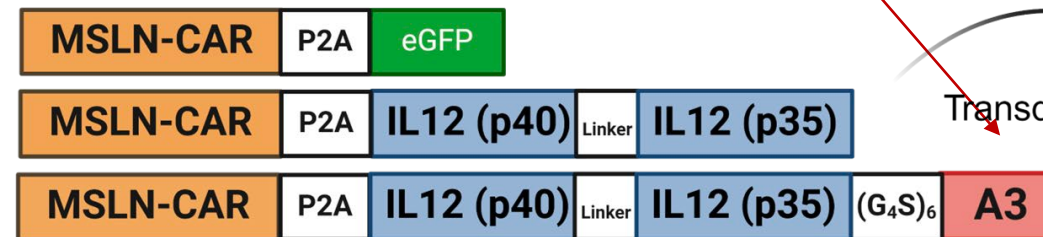
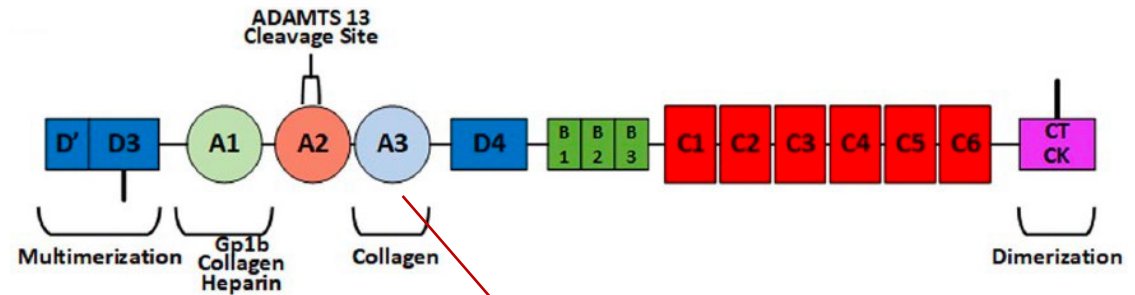
**How can we markedly enhance CAR NK cells
and modulate TME?**

Incorporating tumor matrix directed IL-12 into NK cell CARs

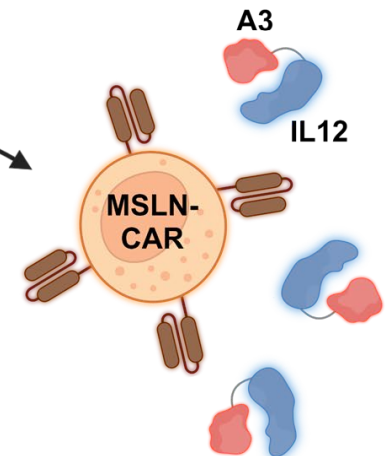
CAR NK vs CAR T secretomes are very different



Fuse A3-domain from vWF to trap IL-12 in TME

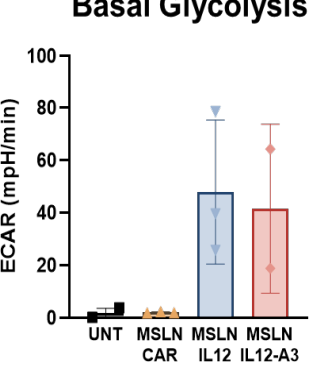
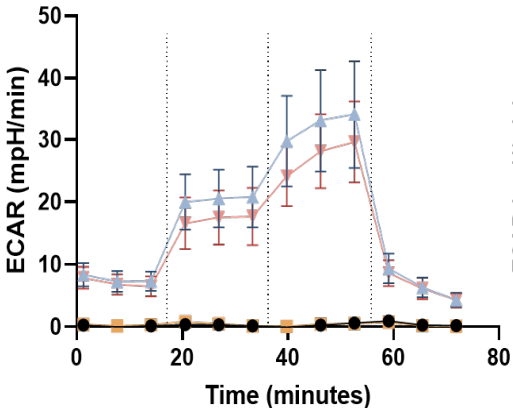
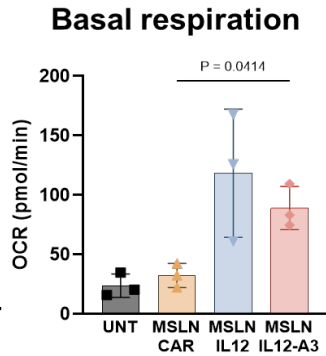
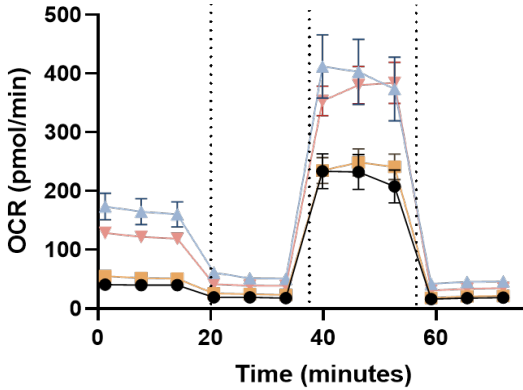
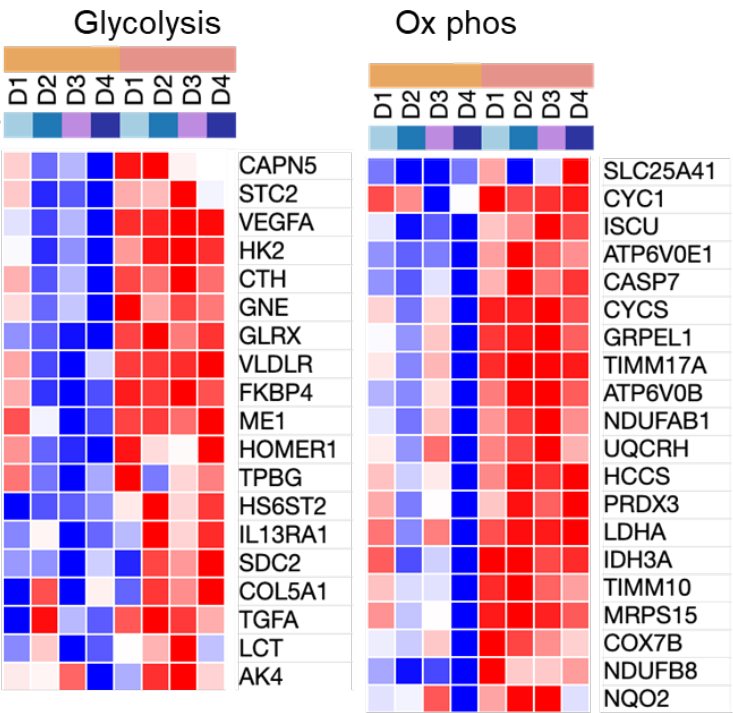
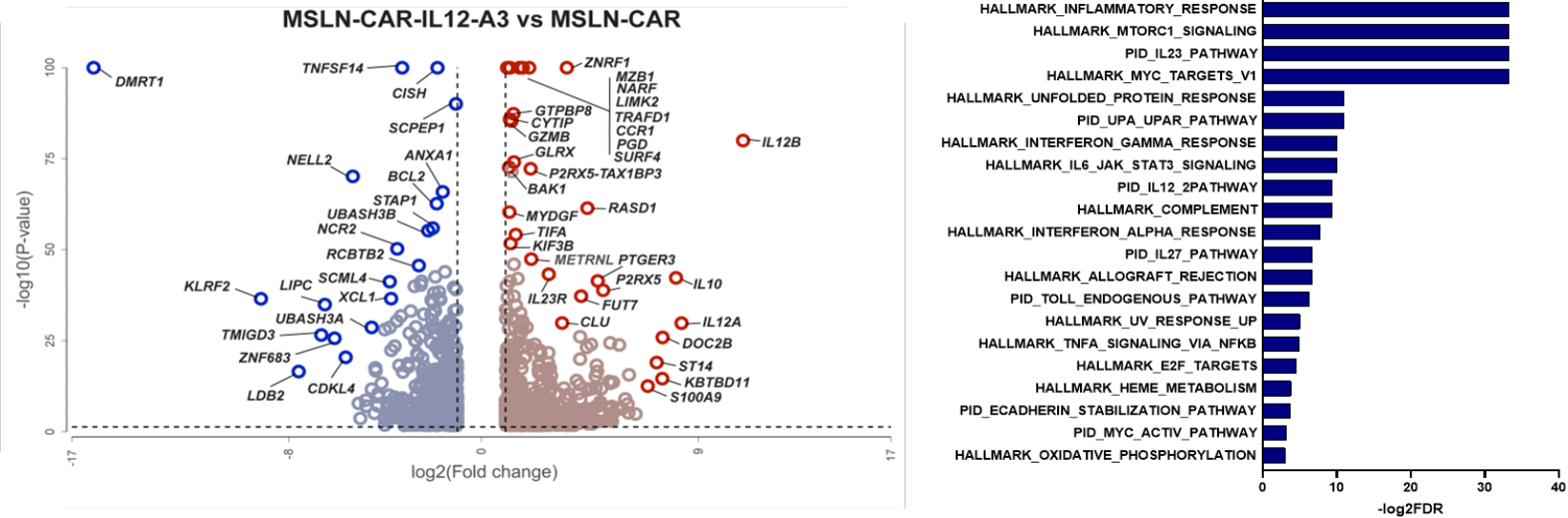


Transduction

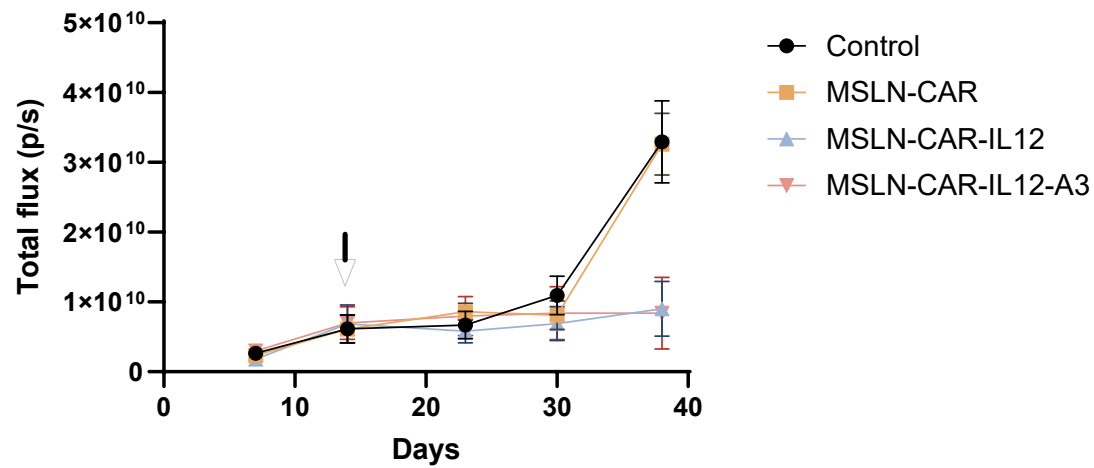
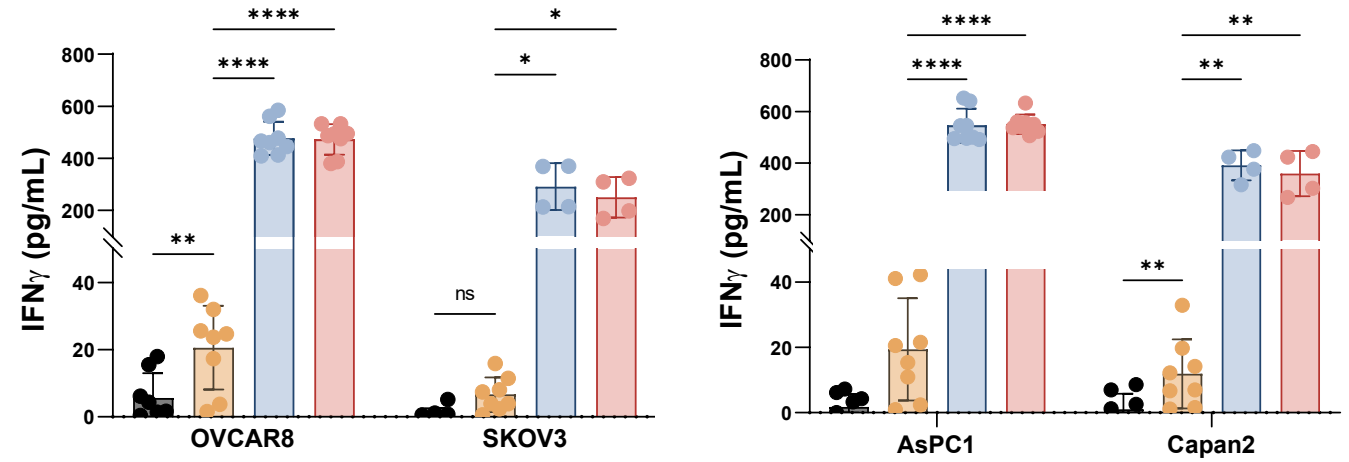
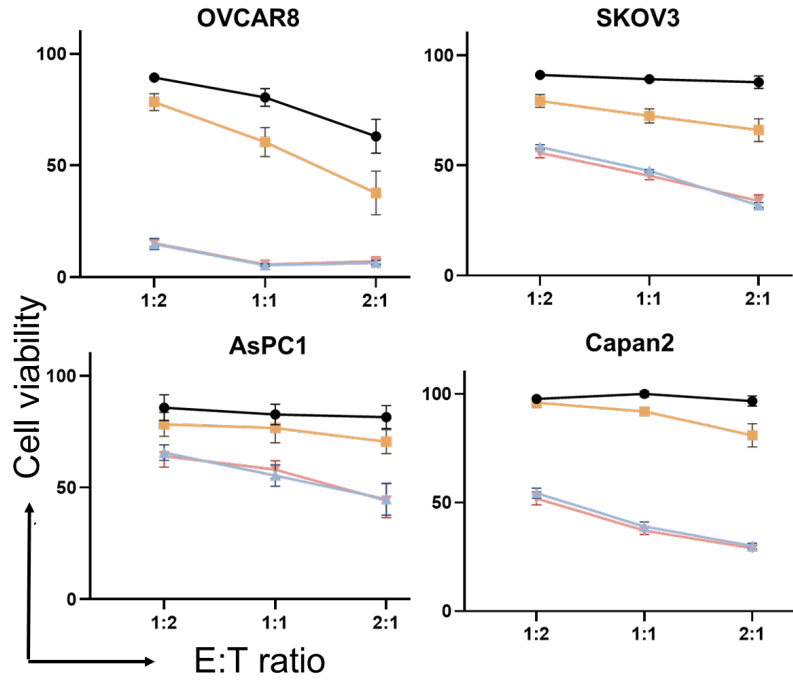


Unpublished data

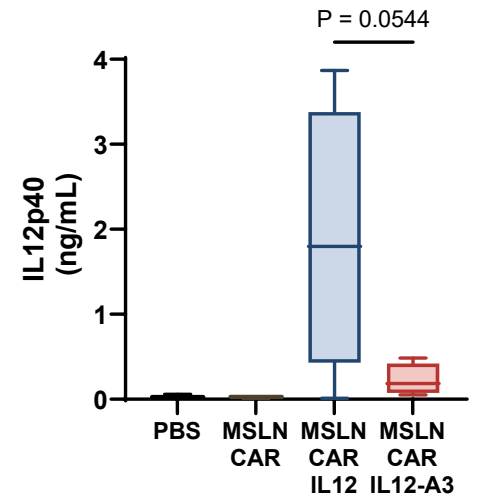
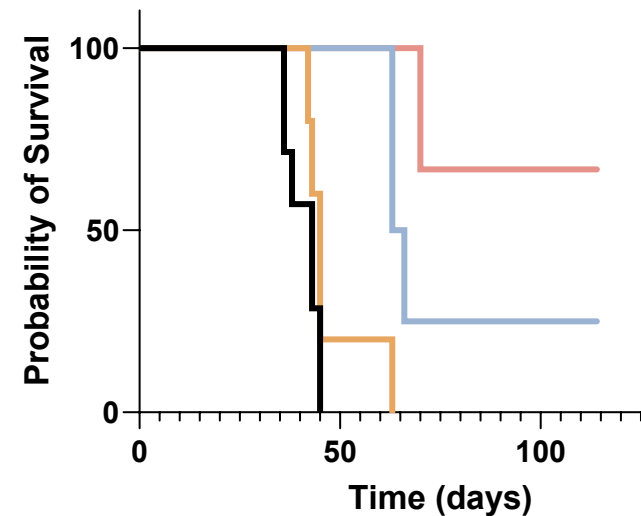
Gene expression and metabolomic changes induced by IL12 engineering in CAR NK cells



Enhanced anti-tumor responses of IL12-engineered CAR-NK cells

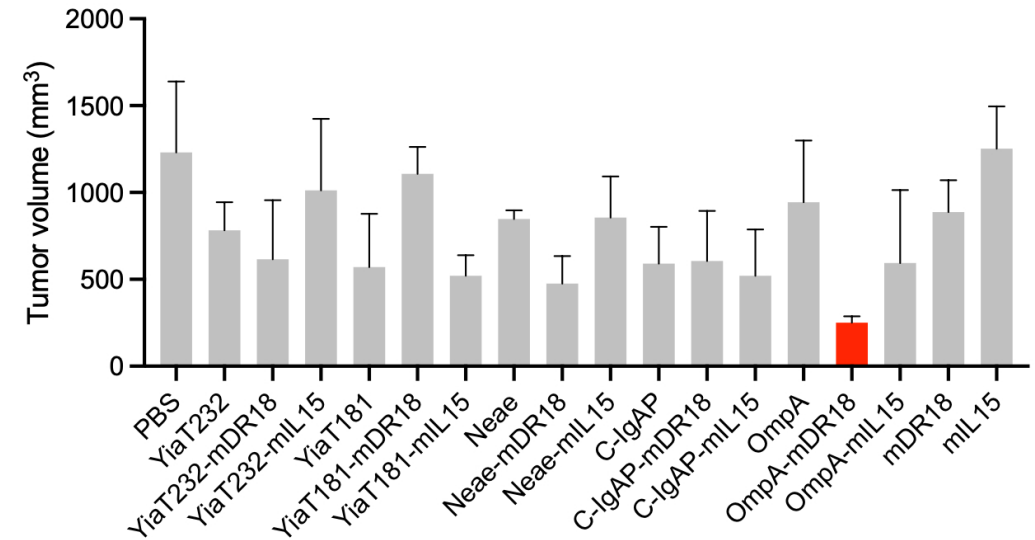
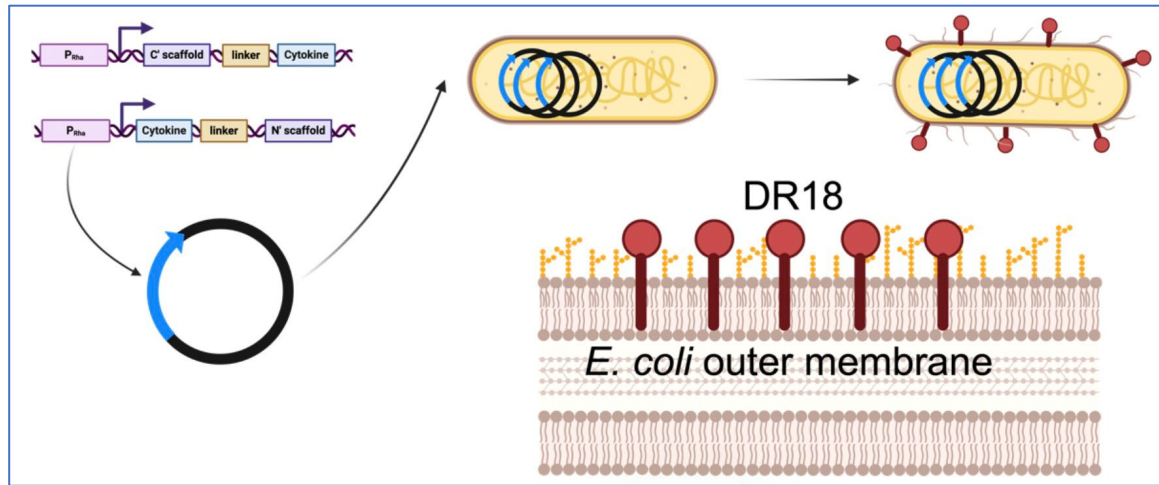


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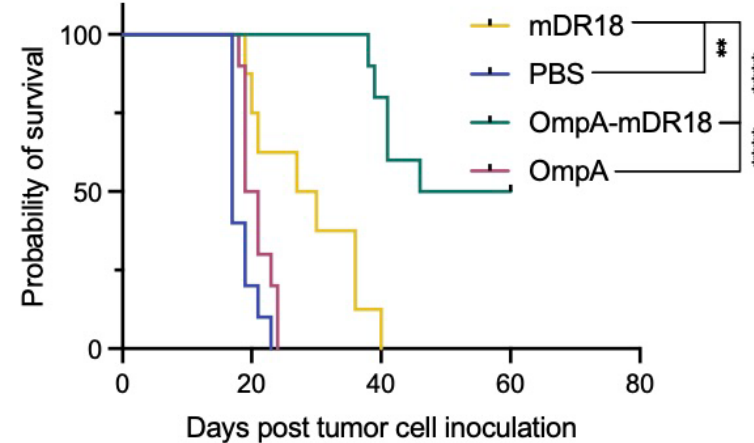
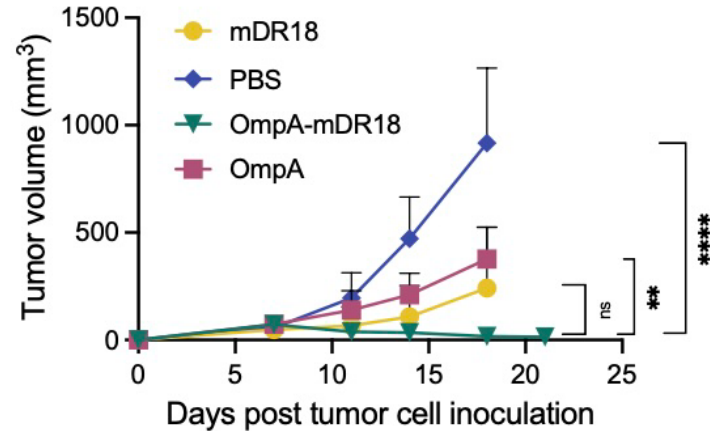


**Can engineer tumor tropic bacteria to deliver
cytokines into TME?**

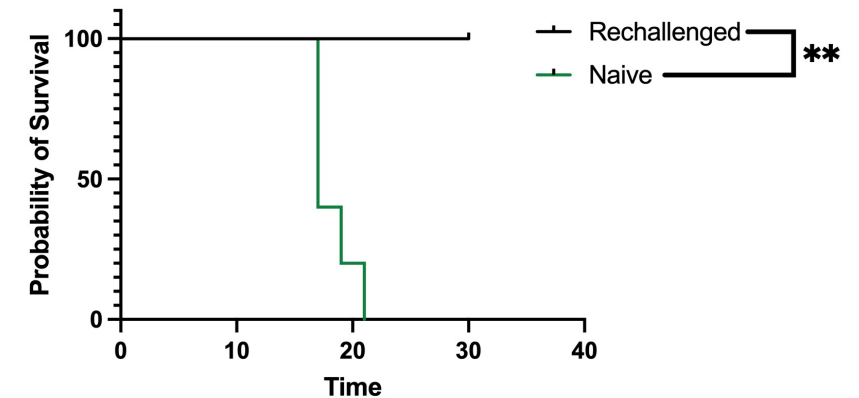
Engineer *E. coli* (K-12 DH5a) to surface display IL-15, IL-18 or IL-21



Tumor control

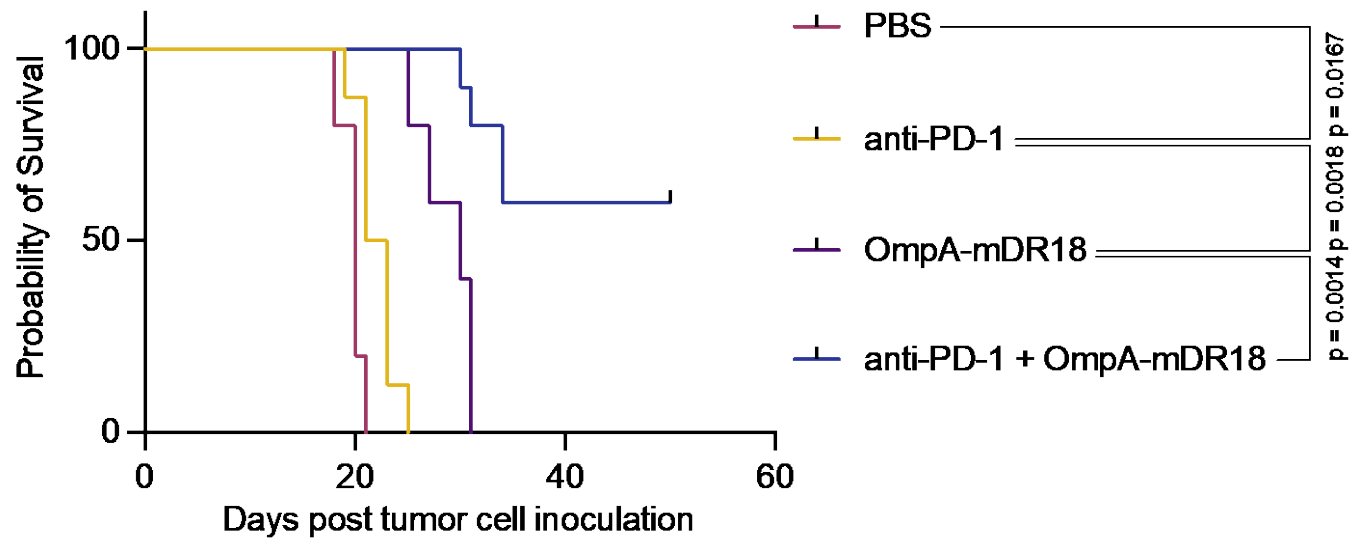
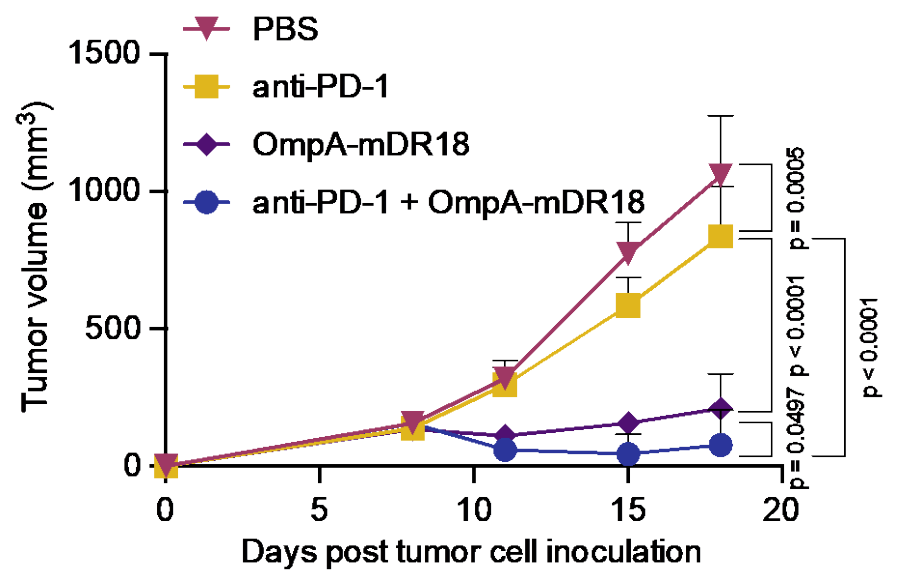
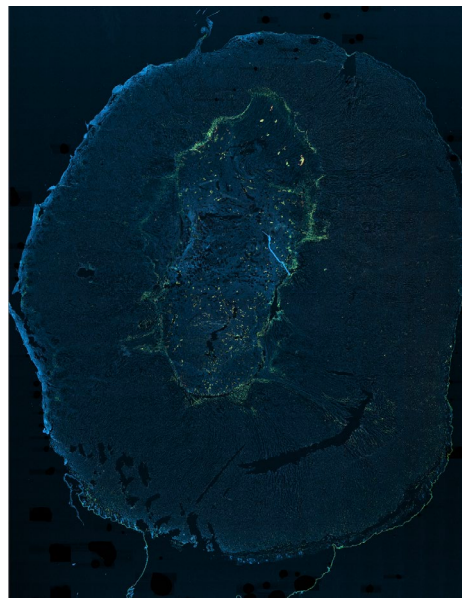
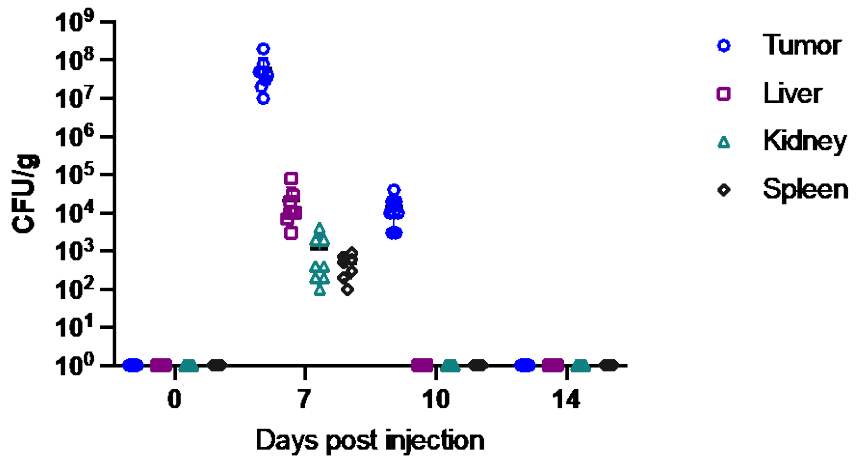
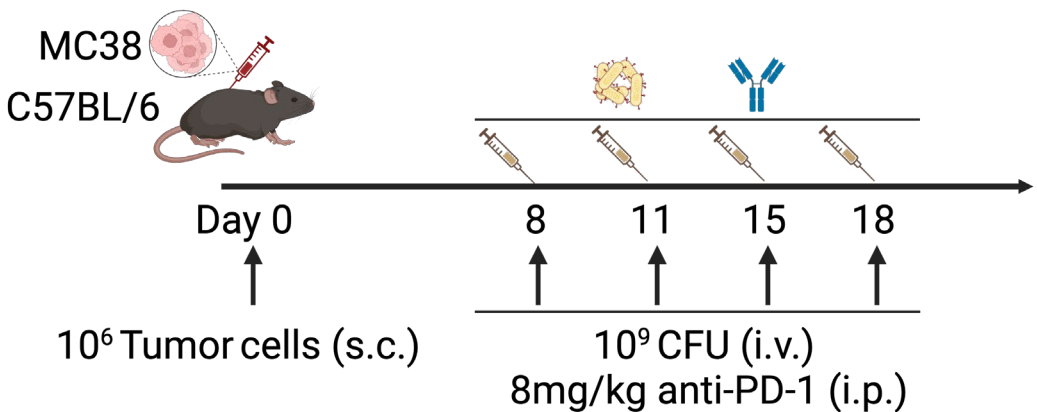


Recall

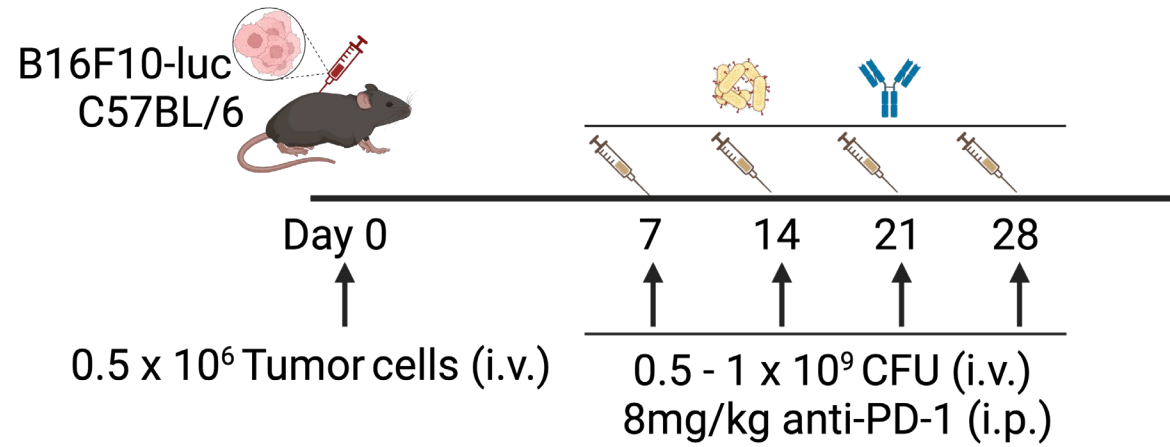


Systemic administration of *E. coli*-mDR18 synergized with anti-PD-1 treatment

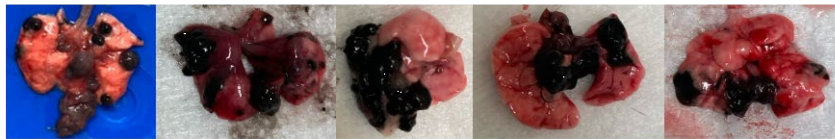
Systemic delivery



E. coli-mDR18 decrease lung metastasis (Melanoma/B16 model)



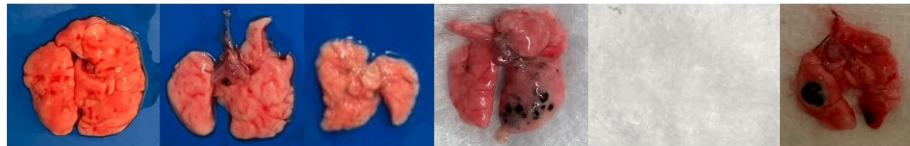
PBS



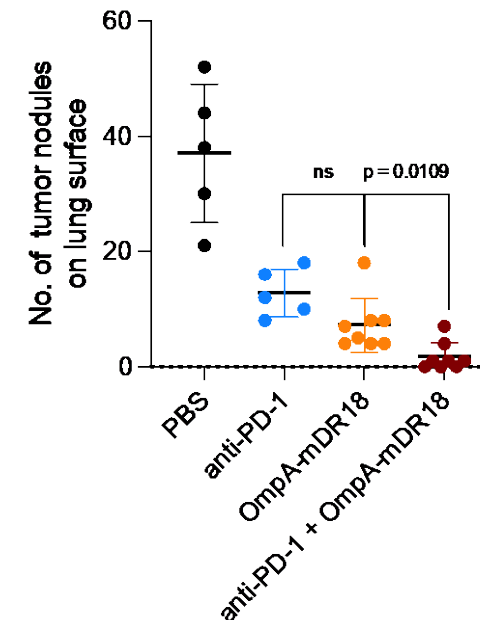
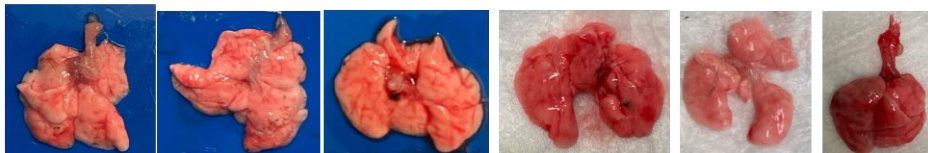
Anti-PD-1



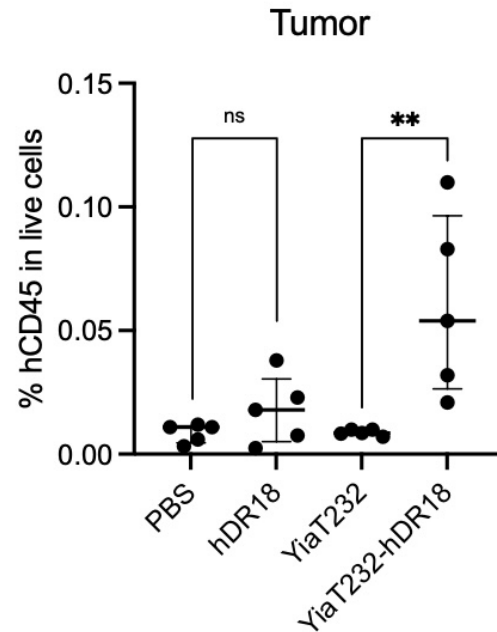
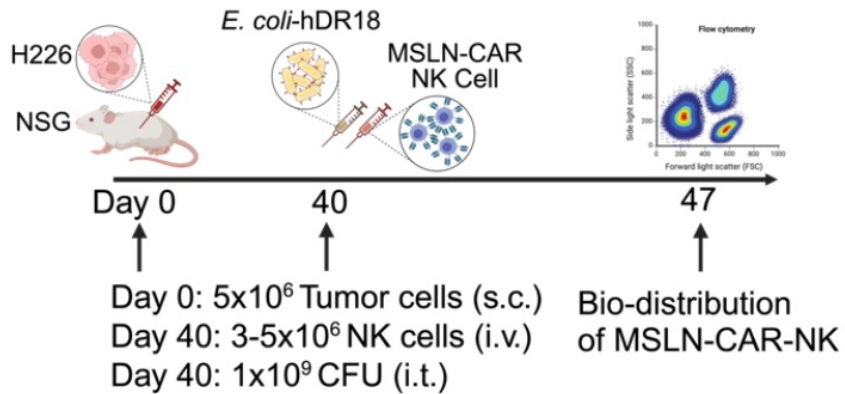
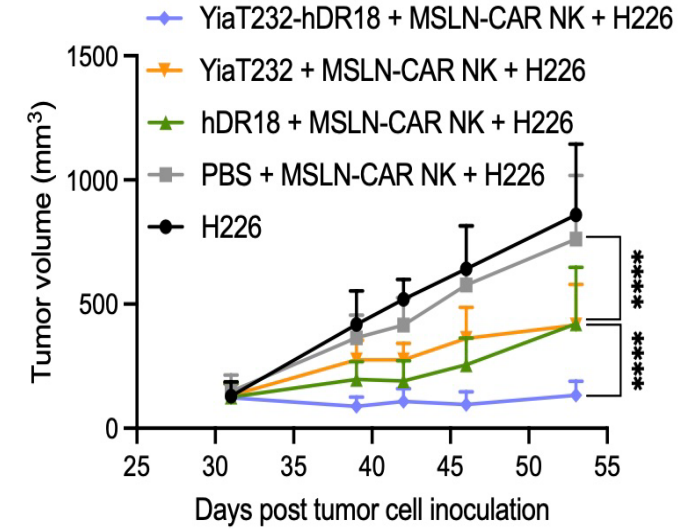
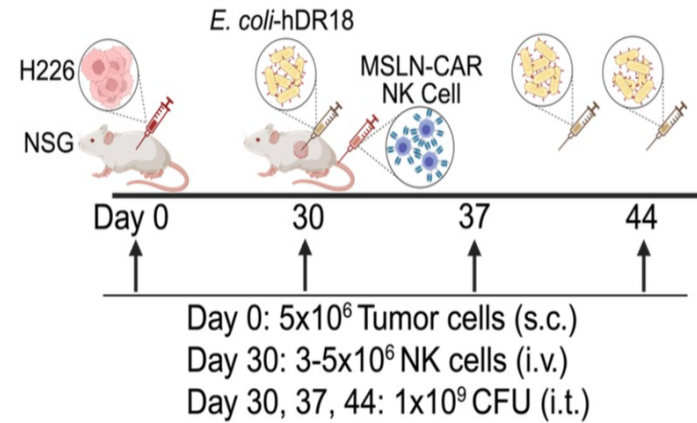
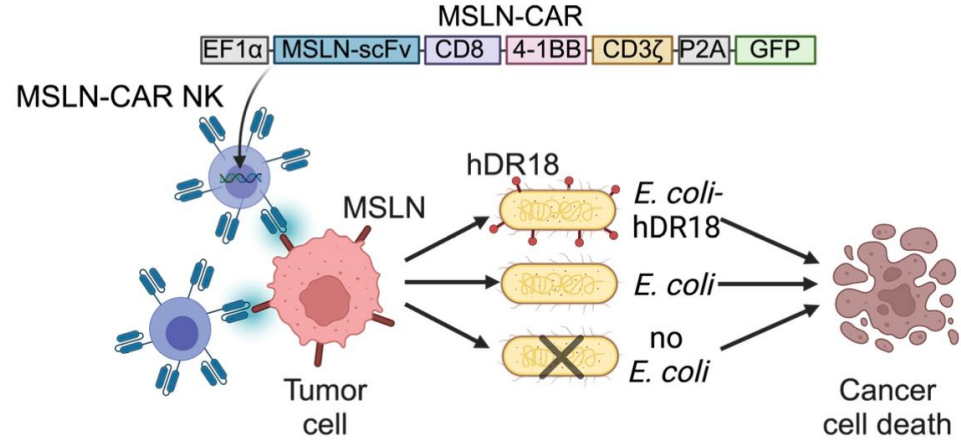
OmpA-mDR18



Anti-PD-1 + OmpA-mDR18



Engineered *E. coli* enhance systemically delivered human CAR NK cells



Acknowledgments

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