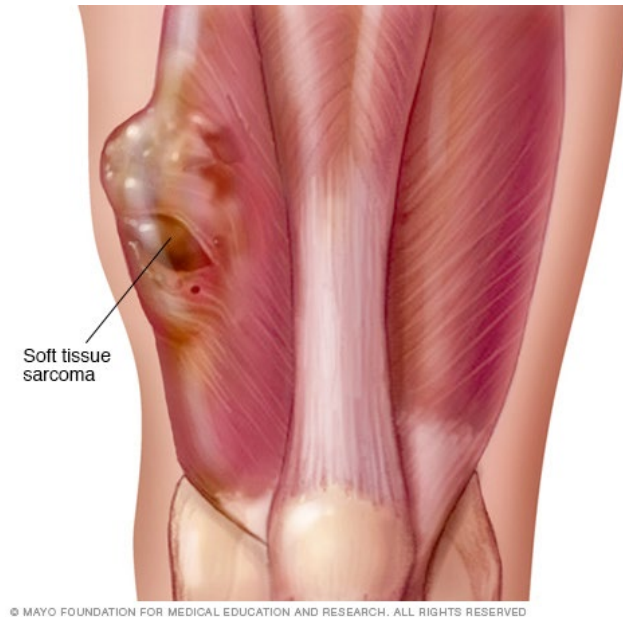


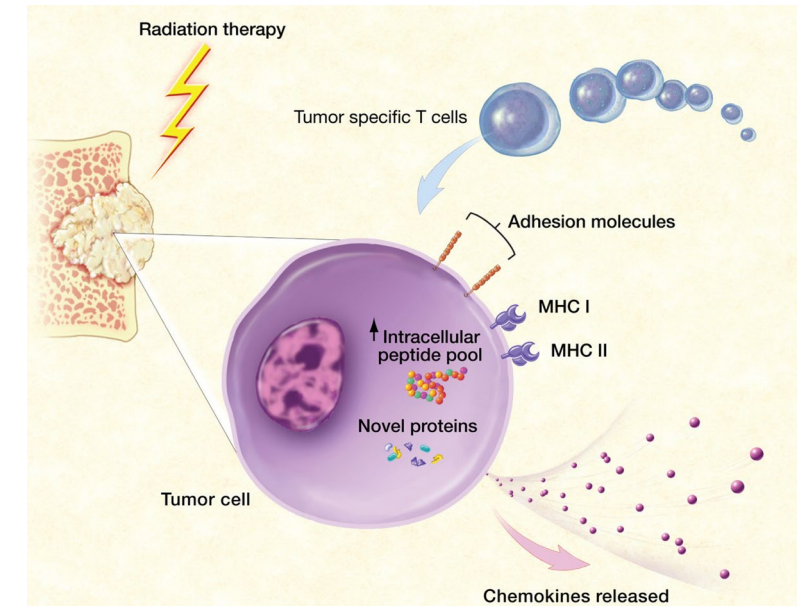
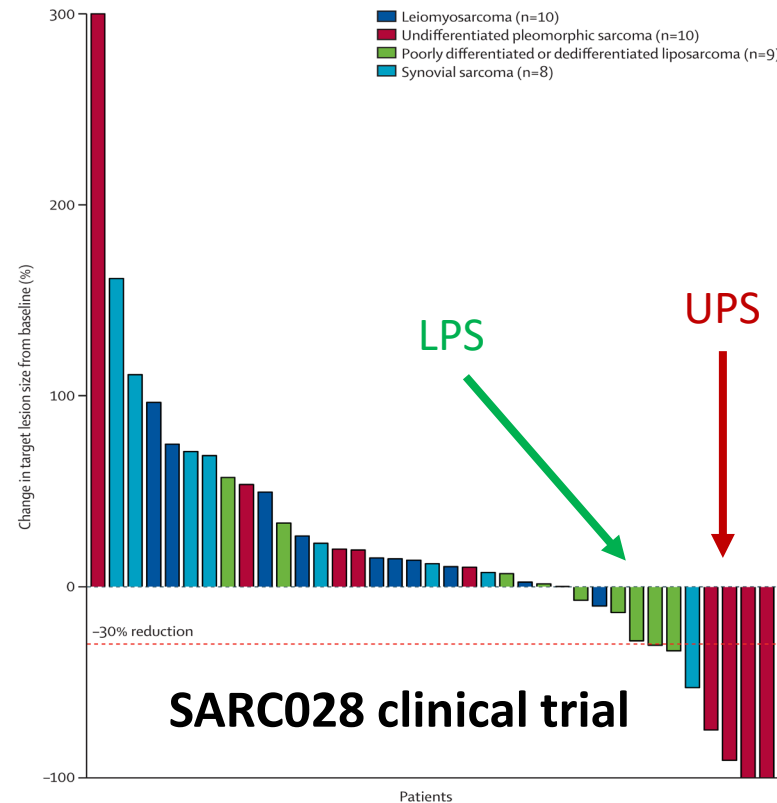
Title: - Co-clinical trial of mouse model of soft tissue sarcoma suggests a beneficial outcome of adding anti-PD1 antibody to the standard of care regimen of radiation followed by surgical resection.

Authors: - R. Patel, Y. M. Mowery, Y. Qi, M. Holbrook, E.S. Xu, C. S. Hong, A. Bassil, N. Williams, J. Everitt, D.G. Kirsch, C.T. Badea.

- ❑ Roughly 15,000 patients are diagnosed with sarcoma each year
- ❑ 50 different sub-types of soft tissue sarcomas – Leiomyosarcoma, Liposarcoma, Undifferentiated pleomorphic sarcomas, Synovial sarcoma, Rhabdomyosarcoma, and more rare types ...
- ❑ Standard of care – surgery accompanied by image-guided irradiation +/- chemotherapy
- ❑ Approximately half of all patients will succumb to disease – metastases

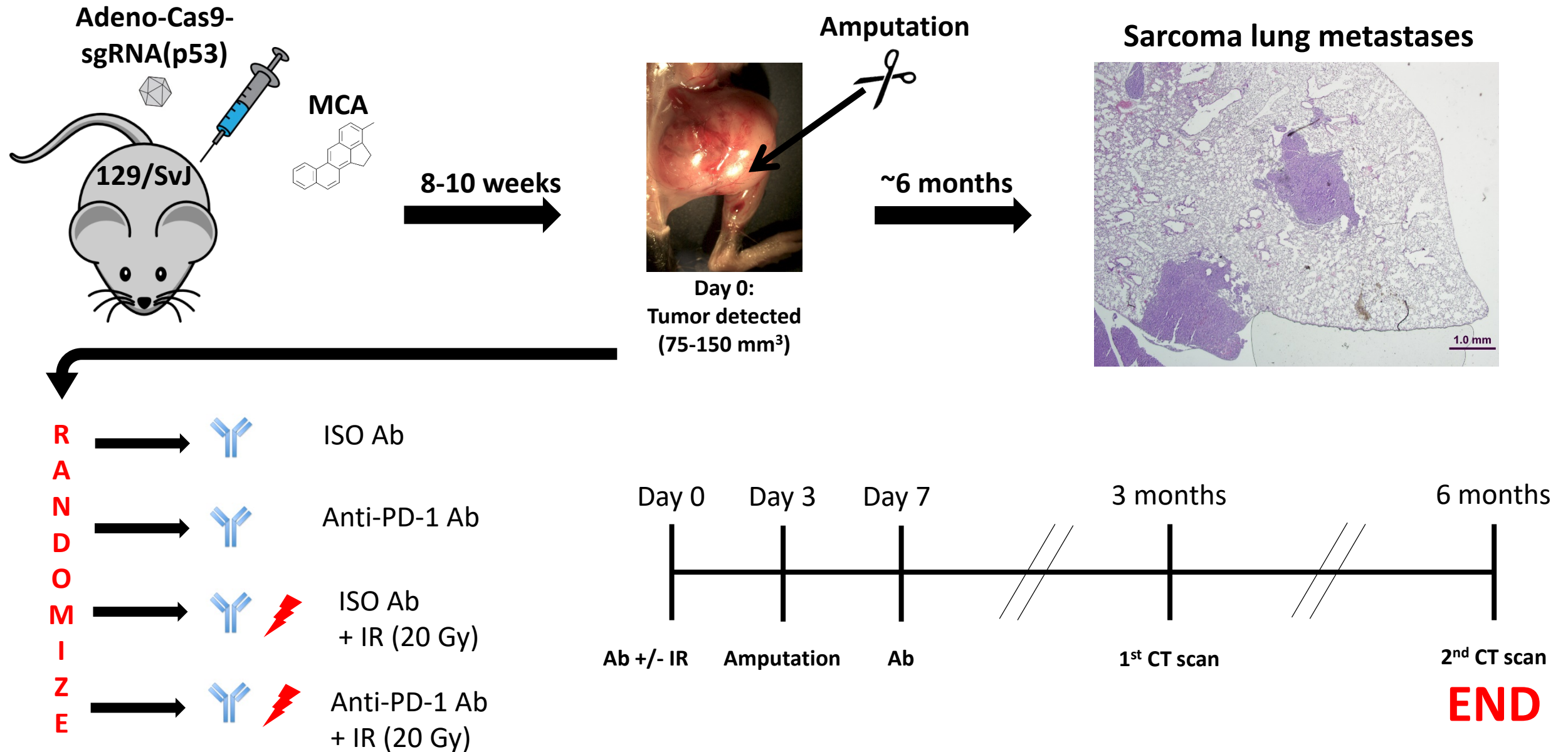


Ognjanovic S., et al, *Cancer* 2009



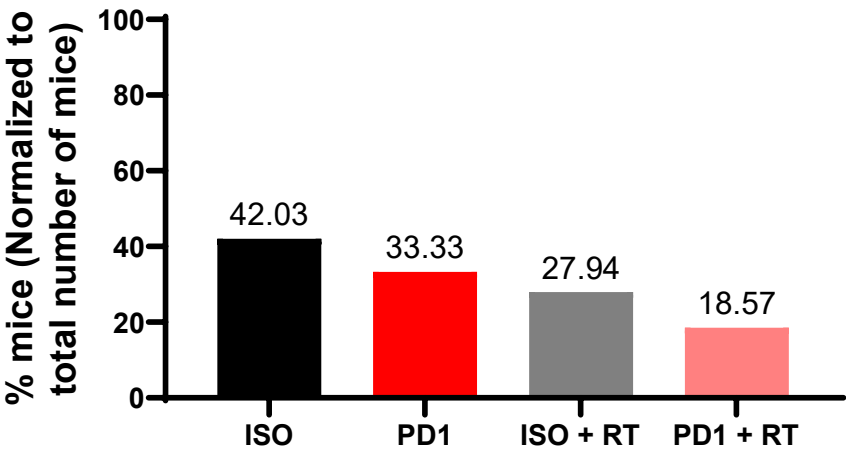
Radiation therapy stimulates immune response

Preclinical sarcoma model of metastatic disease

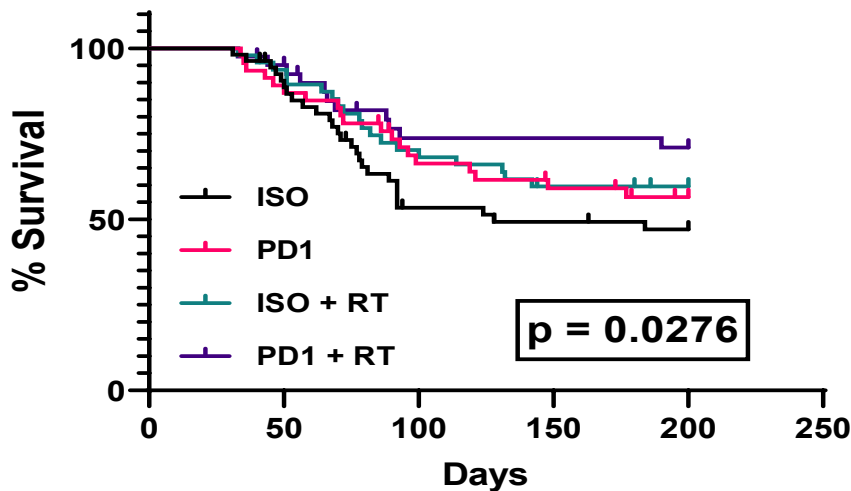


Disease free survival of each cohort of p53/MCA induced sarcoma

Sacrificed due to local recurrence and/or metastases



Disease free survival

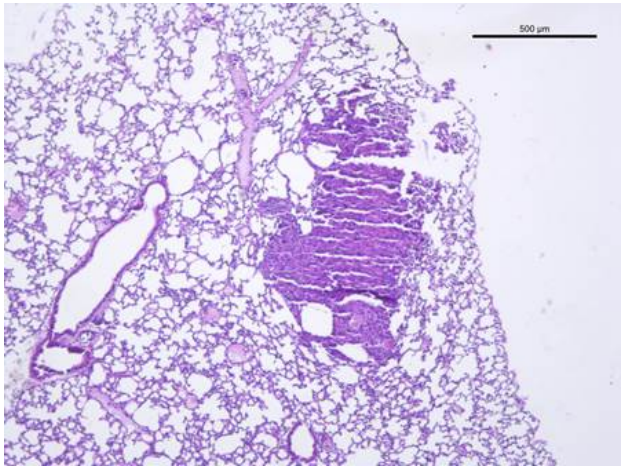


CT-image of lung sarcoma metastases, confirmed by histology

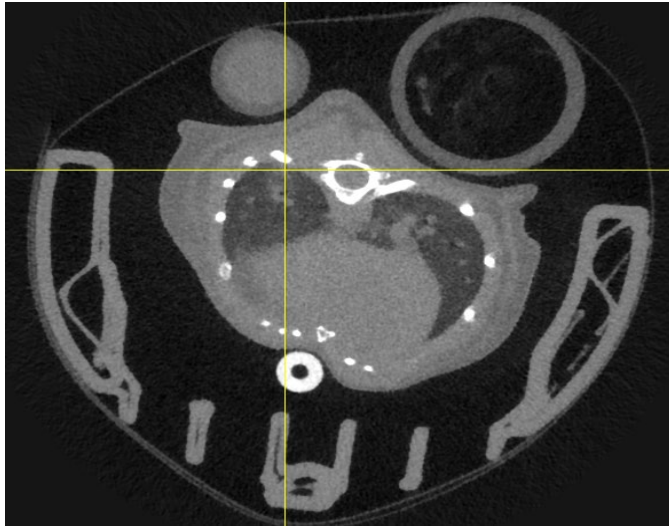


520552 (Sarcoma lung met)

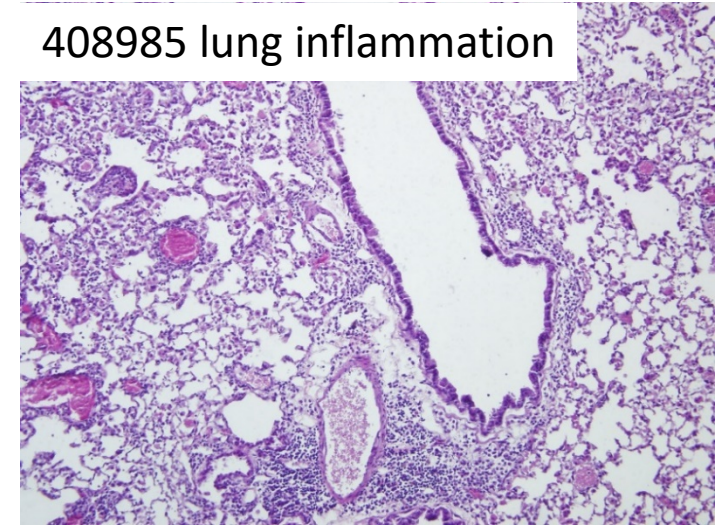
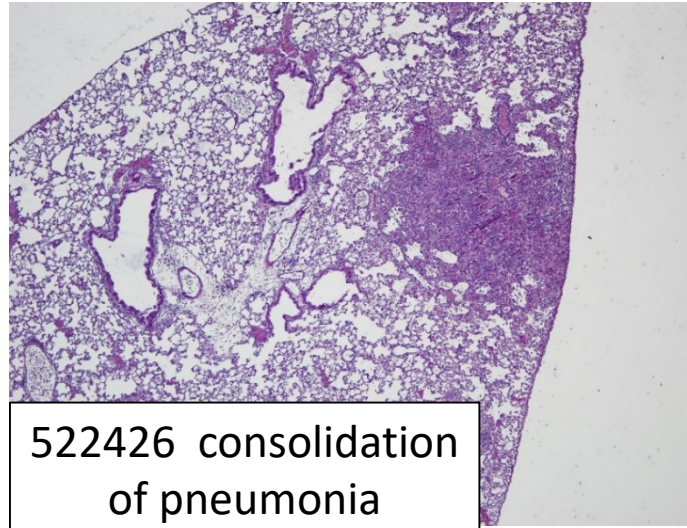
- Detection limit by CT ~ 2 mm
- Not possible to distinguish between different malignancies
- Difficult to separate pneumonitis from lung nodules



Possible lung pneumonitis and non-malignant lesions caused by PD-1 treatment



408290 – PD1 (Pneumonitis)



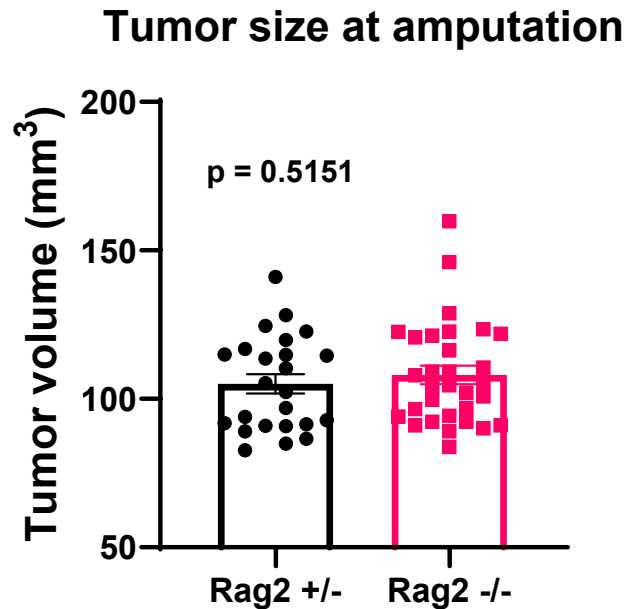
➤ Does PD-1 treatment lead to increase pneumonitis in mice? – On-going analysis....

Treatment groups	# of mice dead/sacrificed/reached end	# of mice sacrificed due to metastases	% mice sacrificed due to metastases
ISO	55	8	14.55
PD1	48	6	12.50
ISO + RT	49	1	2.04
PD1 + RT	43	2	4.65



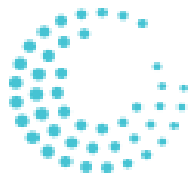
➤ Why low-rate of metastases in untreated group (ISO)? – On-going analysis....

Future experiments to decipher the mechanism of low rate of metastases



- Rag2 KO mice – Does absence of mature B- and T-cells accelerate the rate of metastases?
- Induction of p53/MCA tumors in Cas9 mice – Adeno-sgRNA(p53) + MCA
- Prf1 KO mice – Does deletion of CD8+ T-cells and NK cells accelerate the rate of metastases?
- CRISPR-barcoding approach – look for clonal dynamics in local vs metastases tumor

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