

Immune cells under the influence of metastatic cancer

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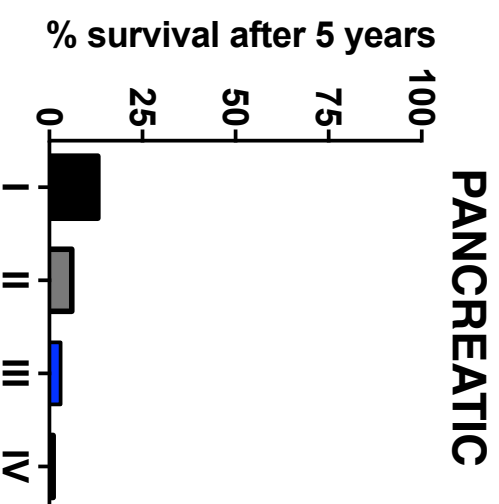
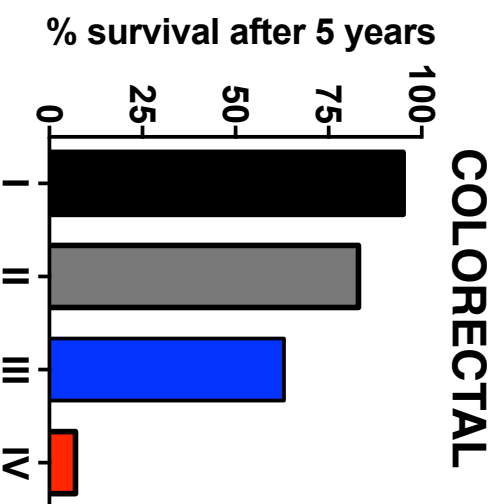
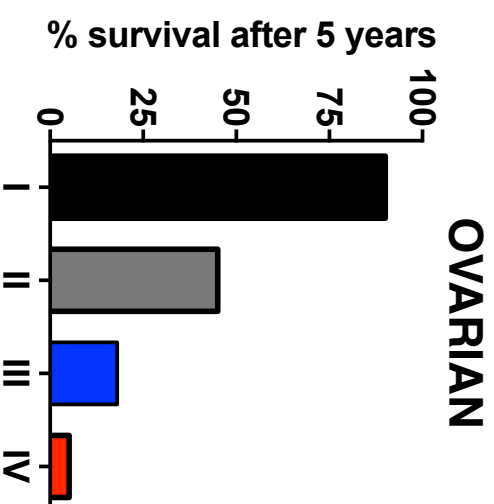
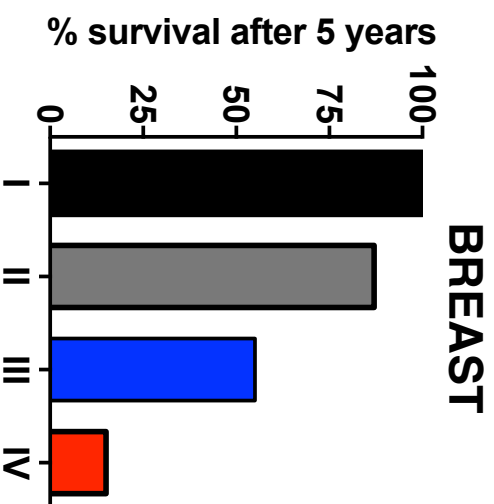
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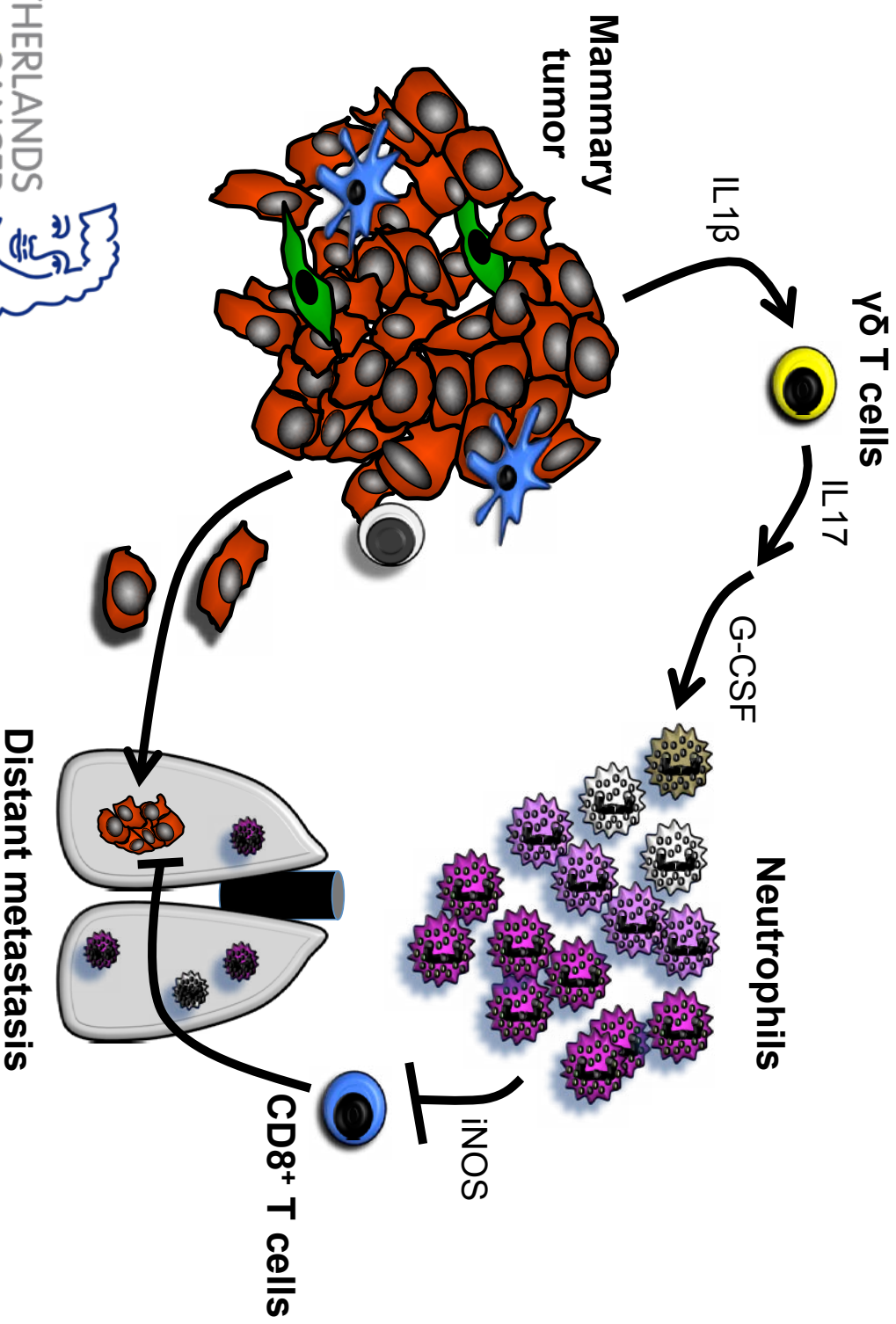


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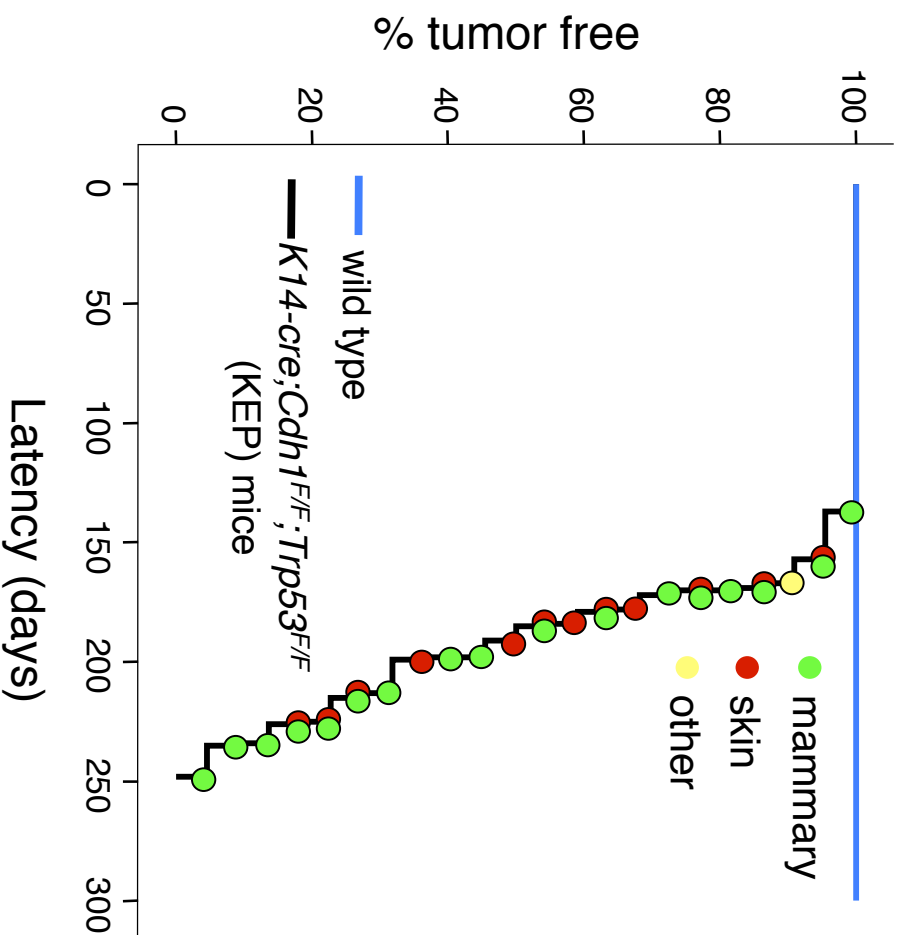
5-year survival rates



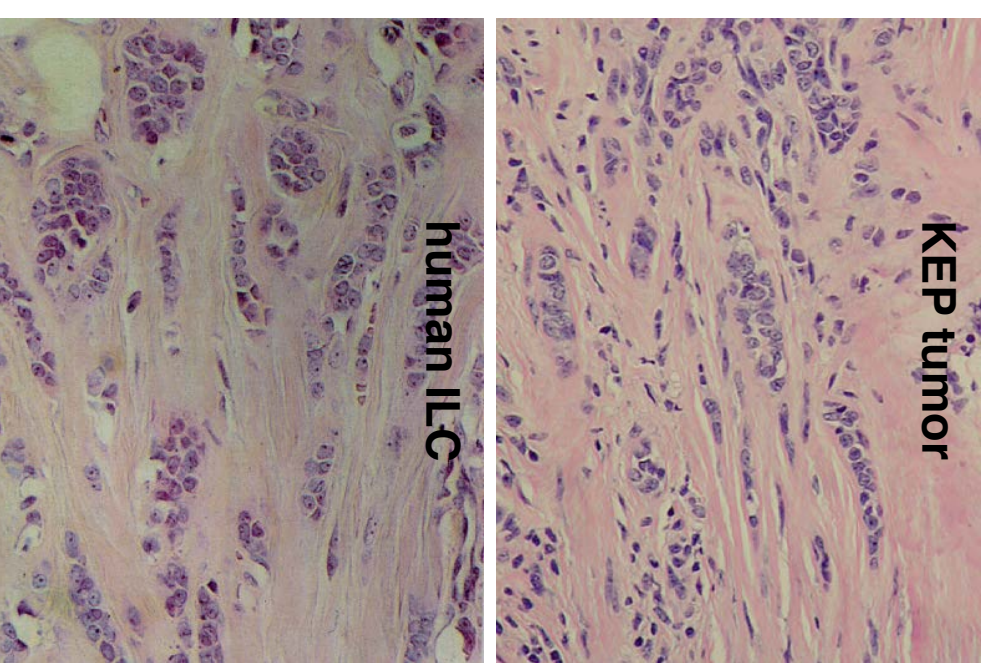
Immune cell dominoes



Invasive lobular carcinoma (ILC) model

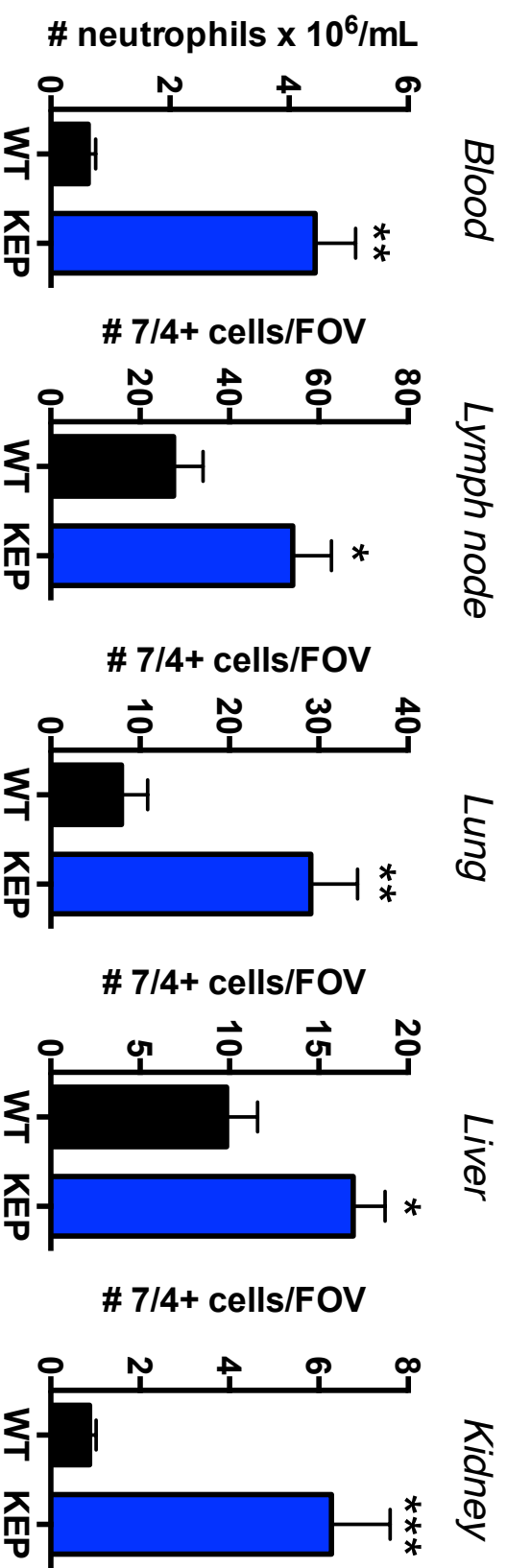
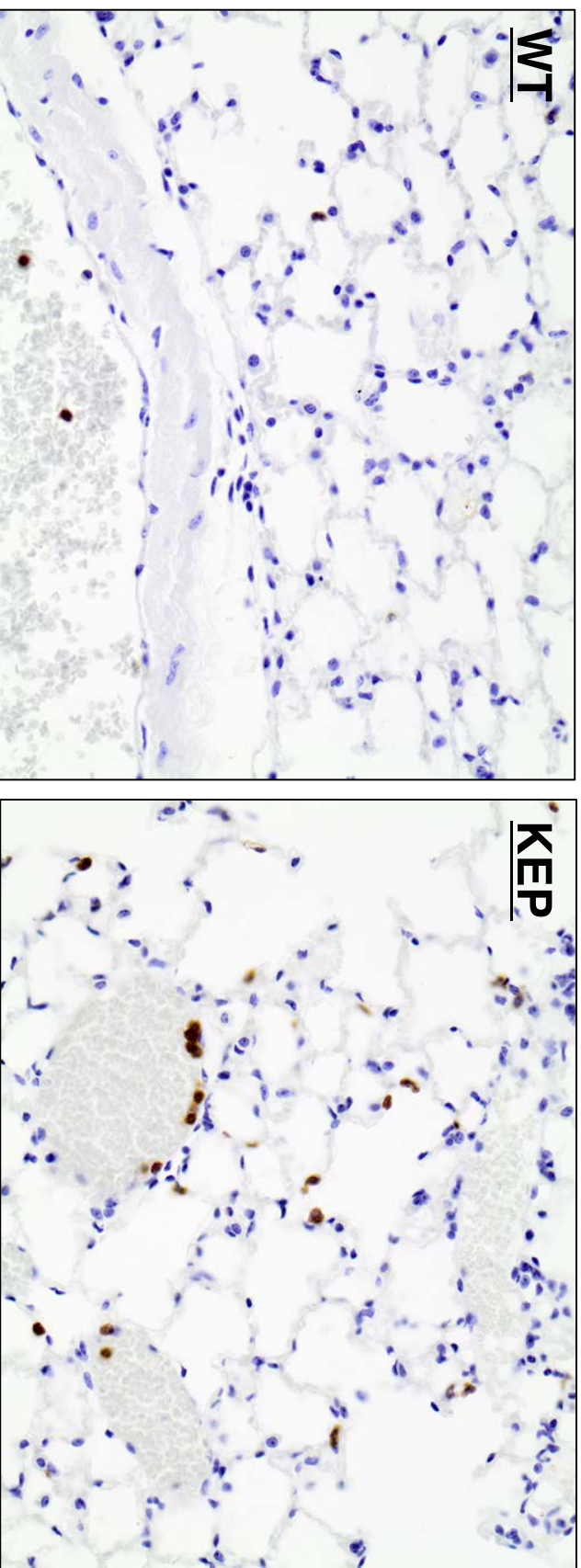


Derksen *et al.*, *Cancer Cell* 2006

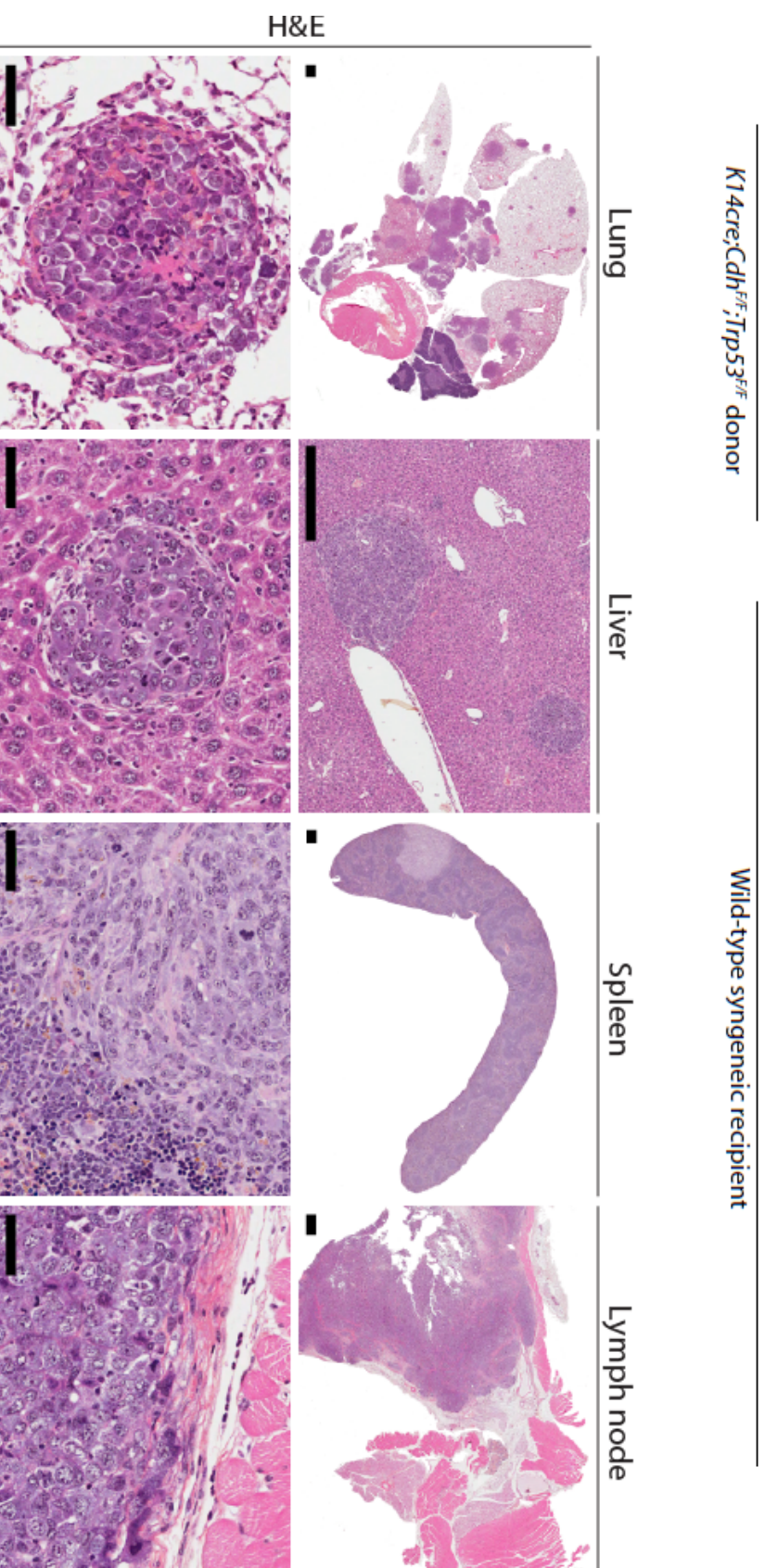
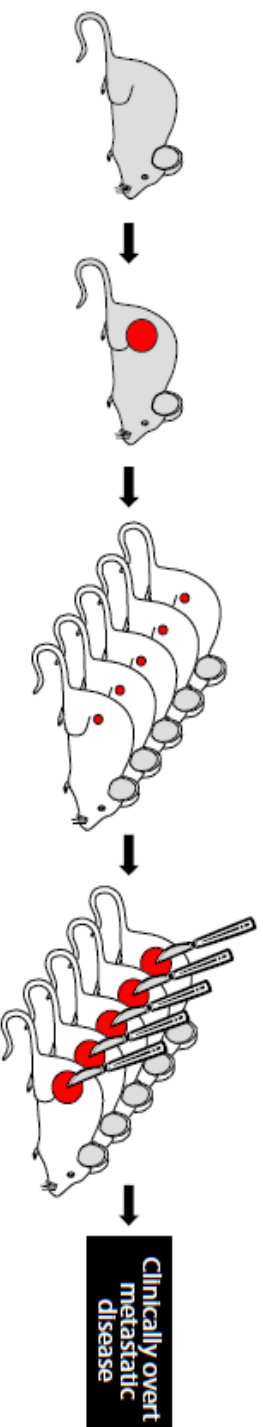


Metastasis formation in LN, lungs, liver

Neutrophils increase systemically in KEP mice

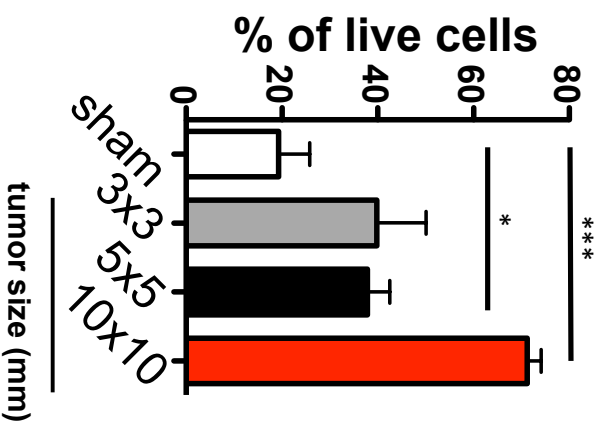


Pre-Clinical Model for Spontaneous Multi-Organ Metastasis Formation



Neutrophil Accumulation in Mammary Tumor-Bearing Mice

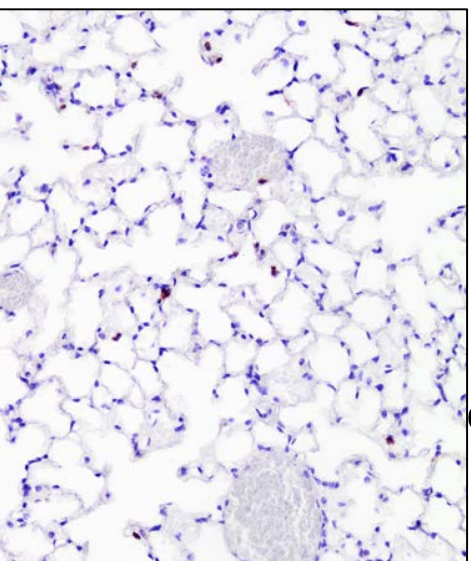
Circulating Ly6G⁺ neutrophils



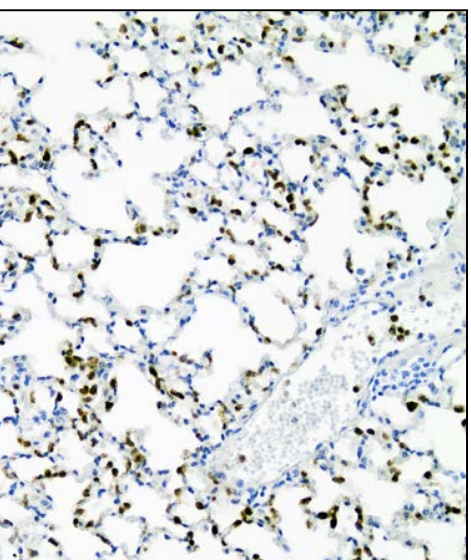
High number of circulating neutrophils in human breast cancer patients is an independent prognostic factor for metastasis formation

(Matsubara et al. 2011; Azab et al. 2012)

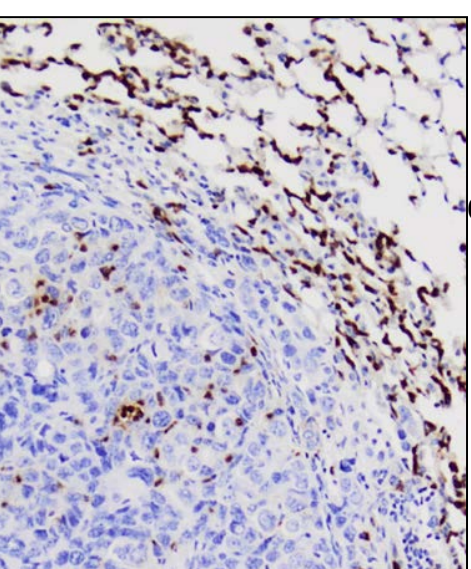
Control Lung



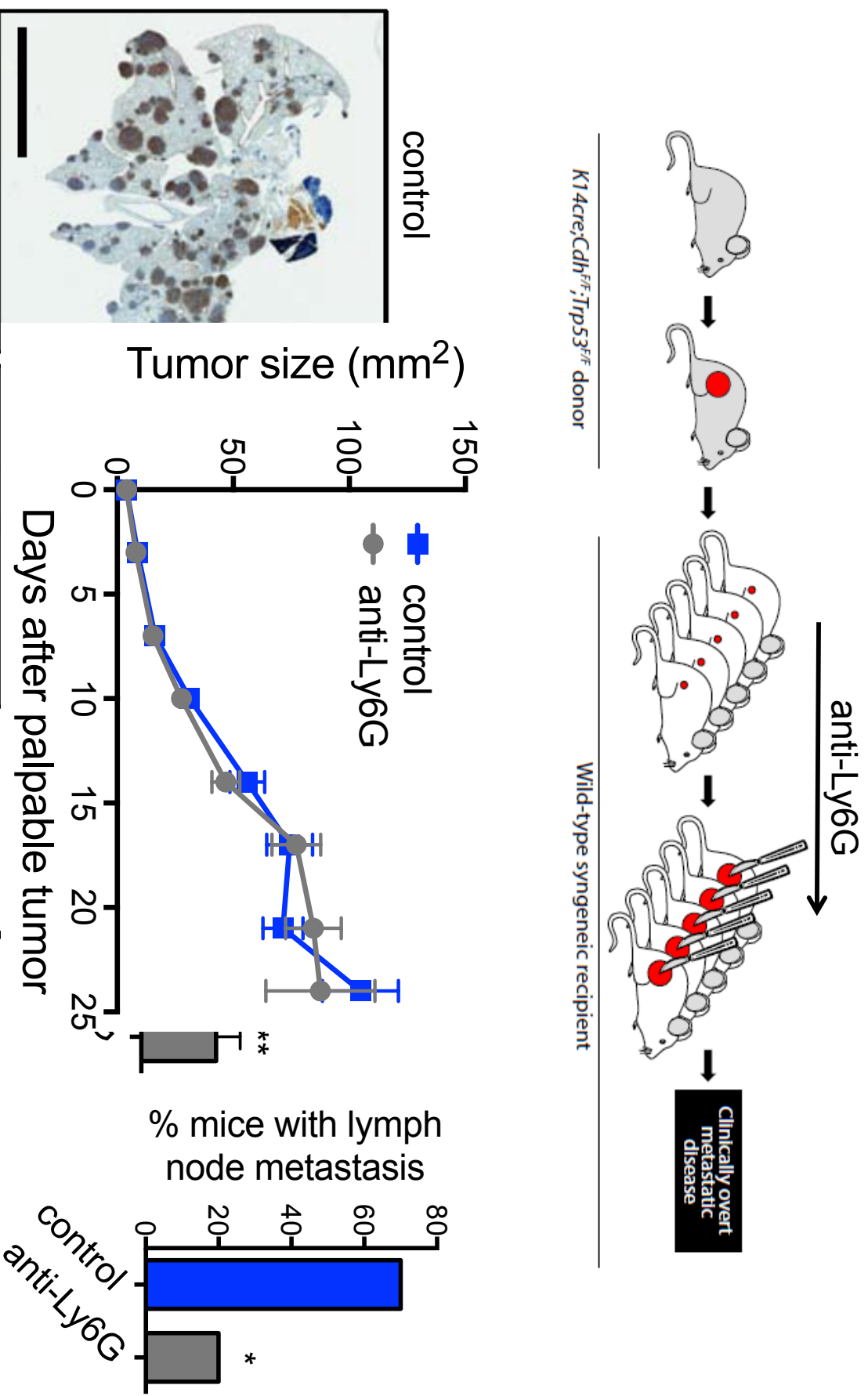
10 x 10 mm



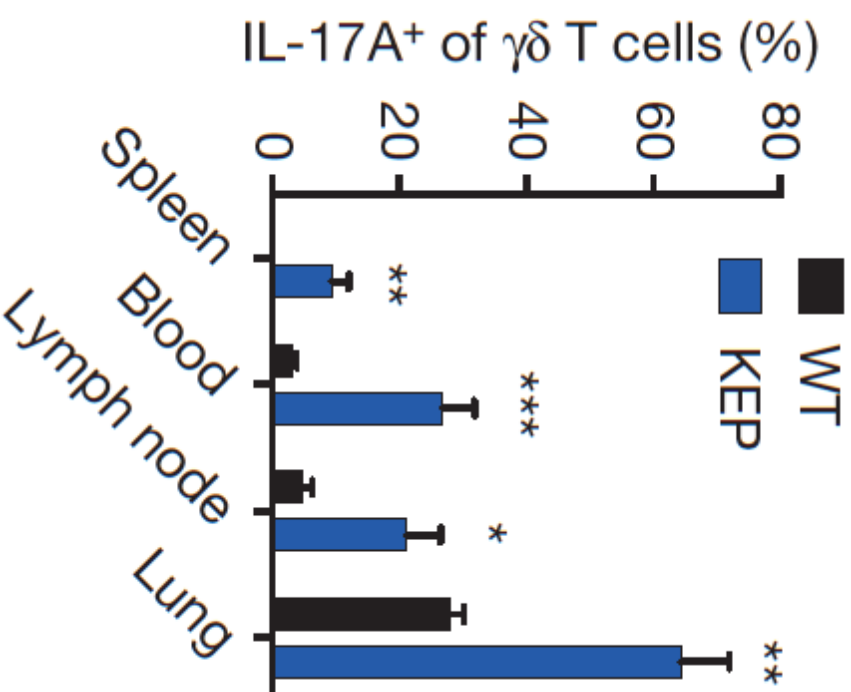
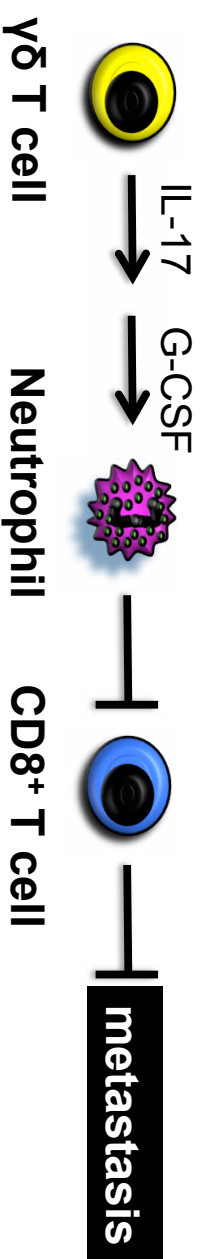
Lung metastasis



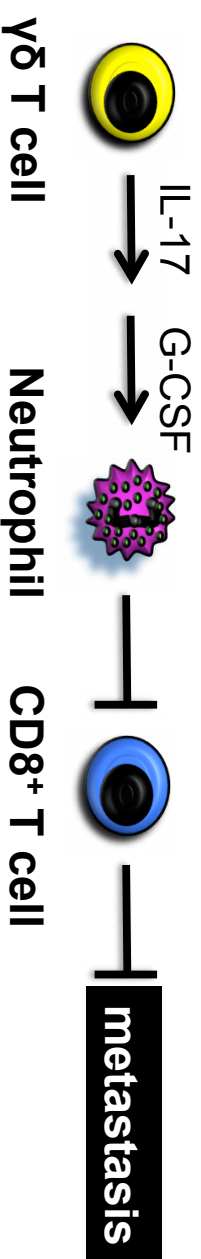
Neutrophils promote multi-organ metastasis formation



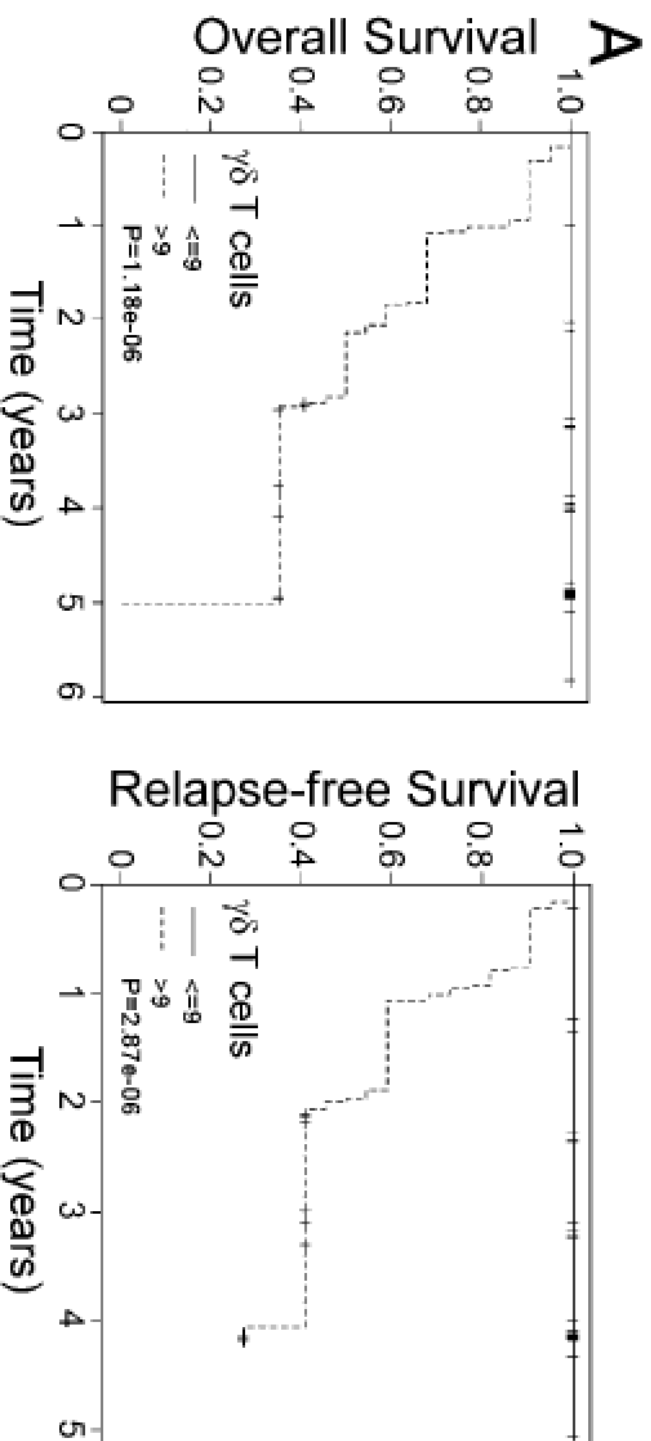
The $\gamma\delta$ T cell/IL-17/G-CSF axis regulates neutrophil expansion



The $\gamma\delta$ T cell/IL-17/G-CSF axis regulates neutrophil expansion

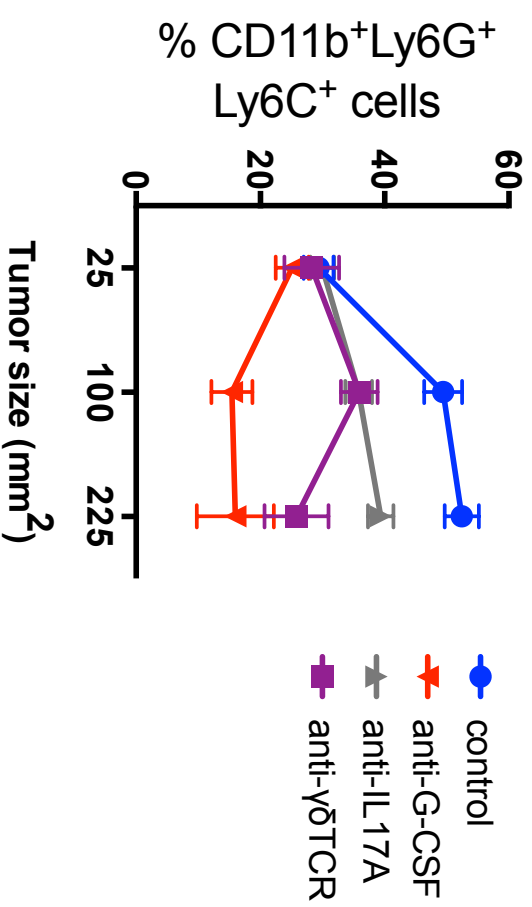
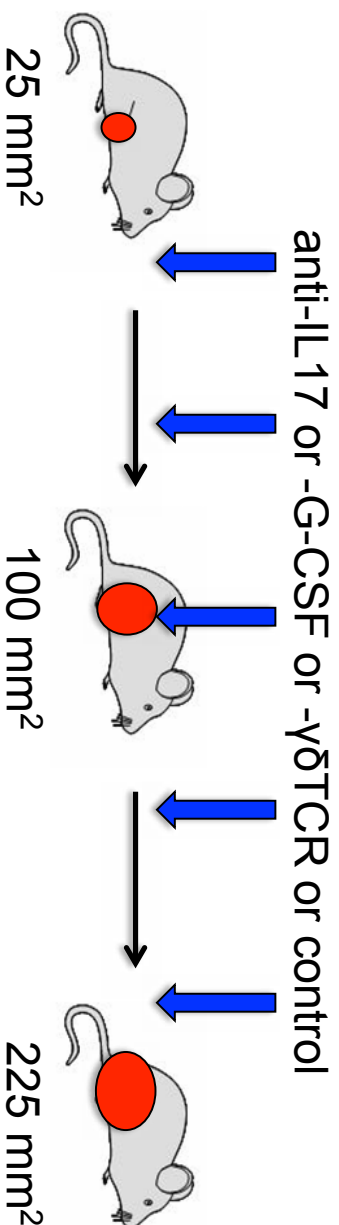


Coffelt et al., *Nature* 2015

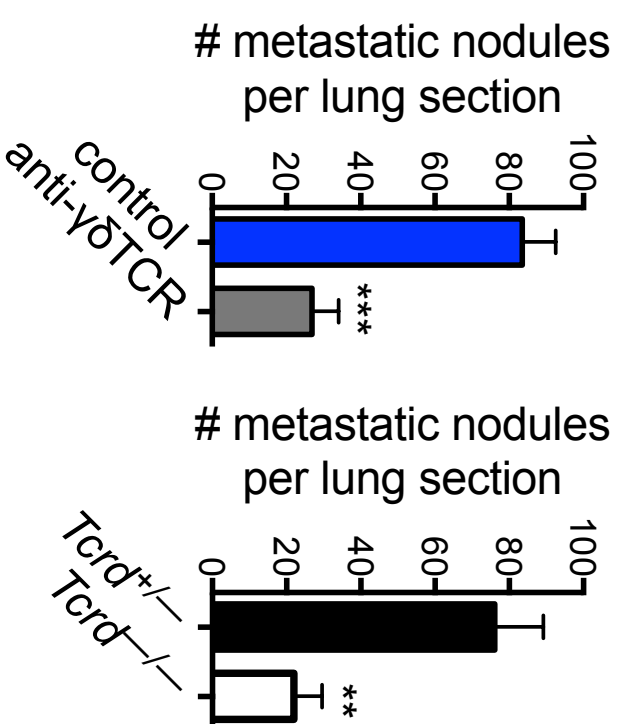
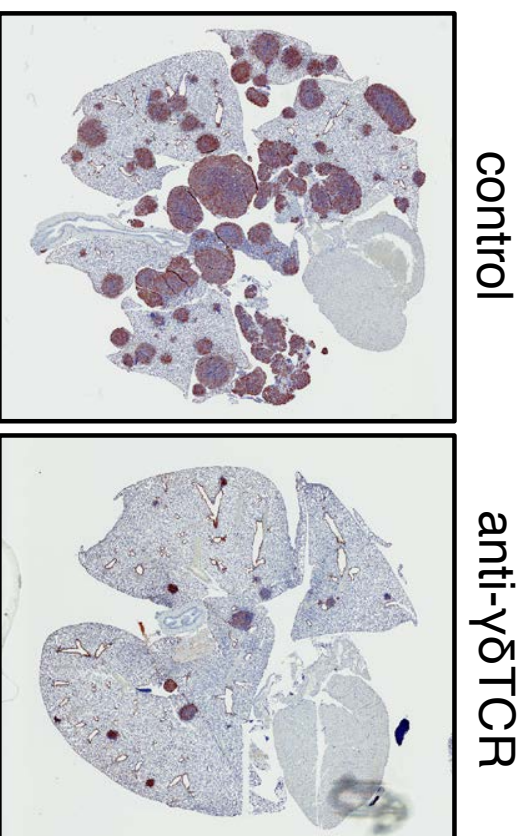
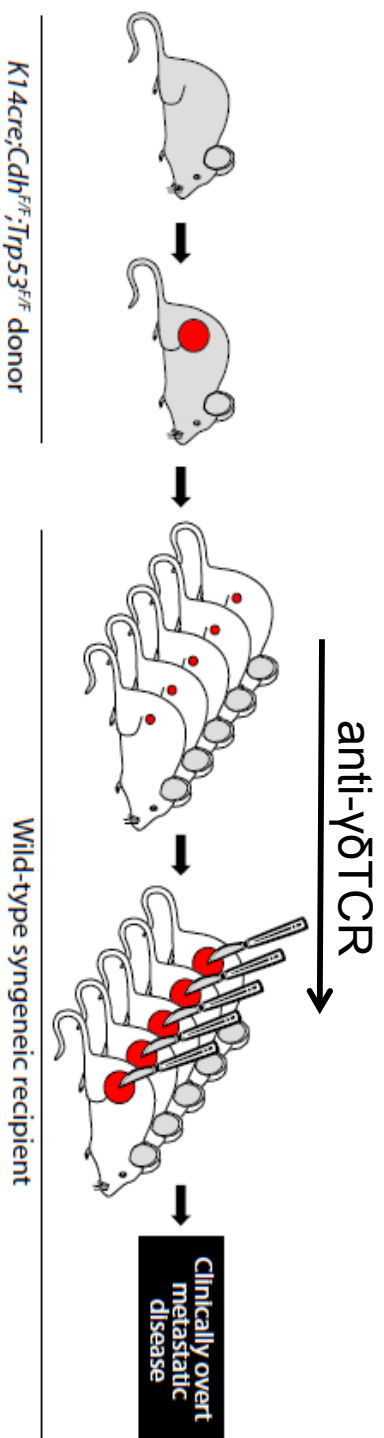


Ma et al., *J of Immunology* 2012

The IL17/G-CSF axis regulates neutrophil expansion



IL17-producing $\gamma\delta$ T cells regulate pro-metastatic neutrophils



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Future directions: metastasis & immunotherapy

- Immune cells both promote and protect against metastasis
(Quail & Joyce 2013 *Nature Medicine*; Kitamura 2015 *Nature Reviews Cancer*)
- 85% of new drugs fail in Phase I/II clinical trials
(Ledford 2011 *Nature*)

