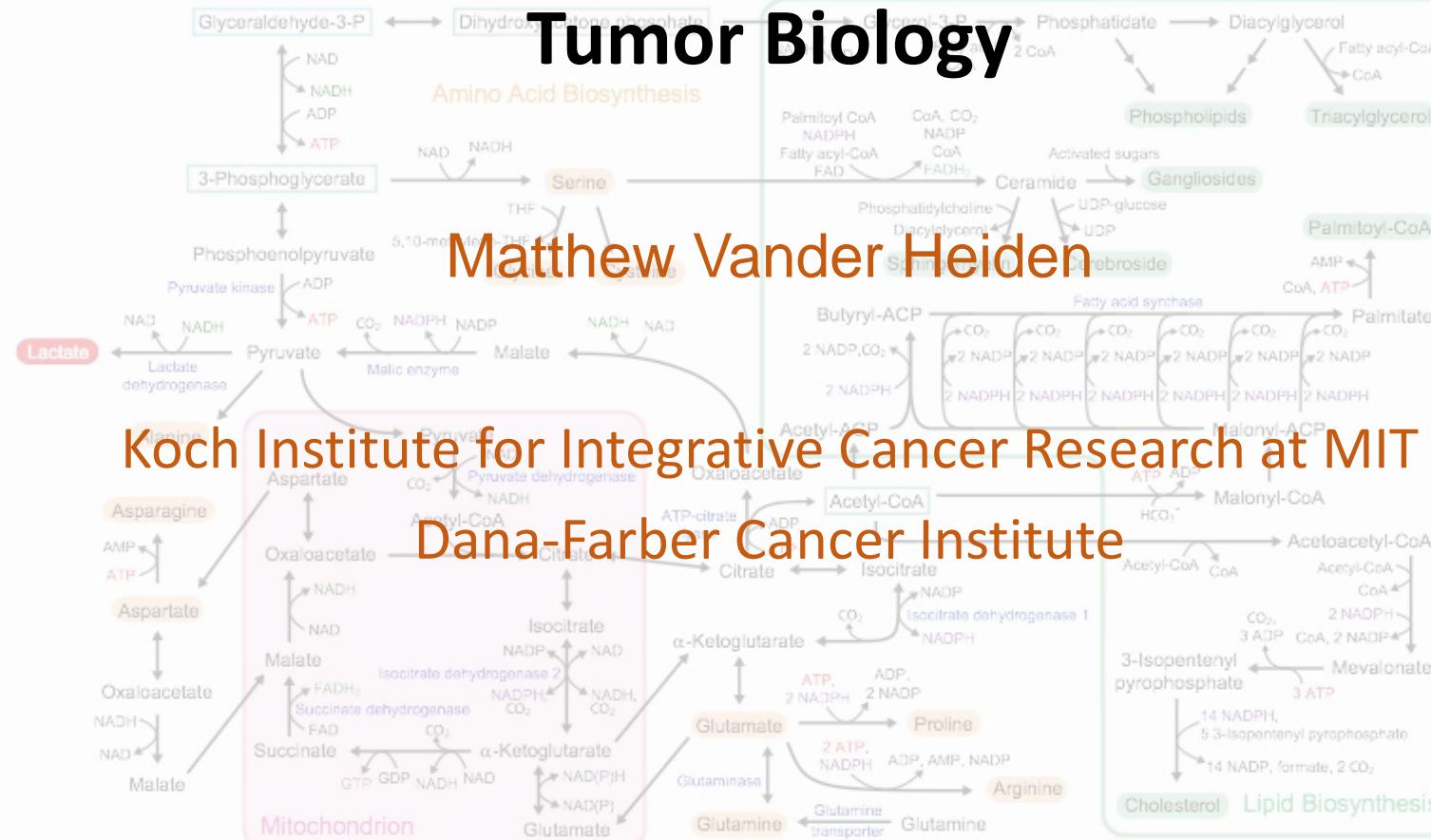


Impact of Extracellular Nutrients on Tumor Biology

Matthew Vander Heiden

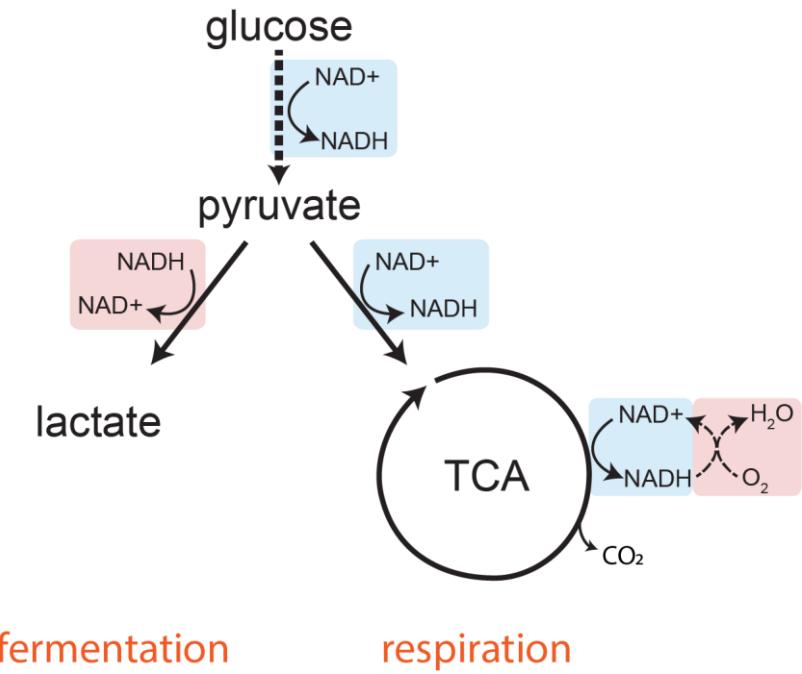
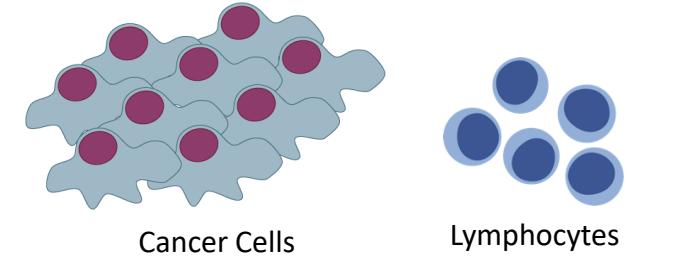
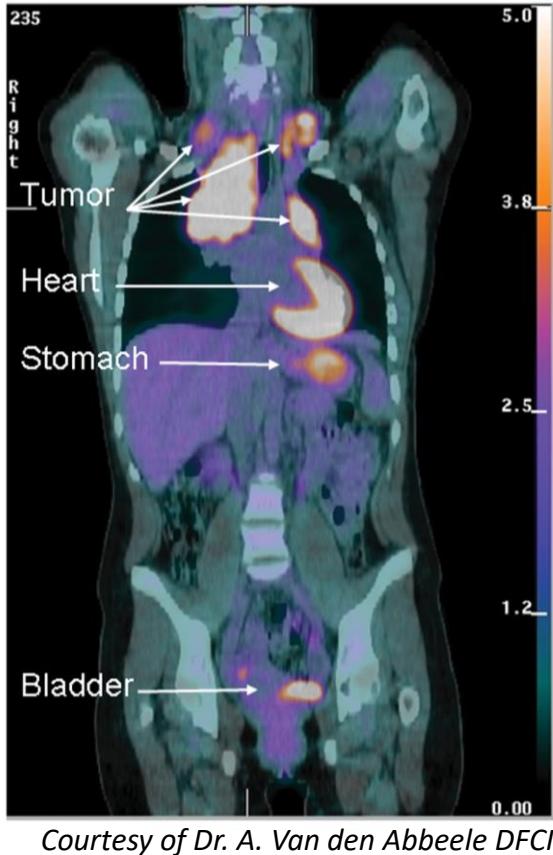
Koch Institute for Integrative Cancer Research at MIT
Dana-Farber Cancer Institute



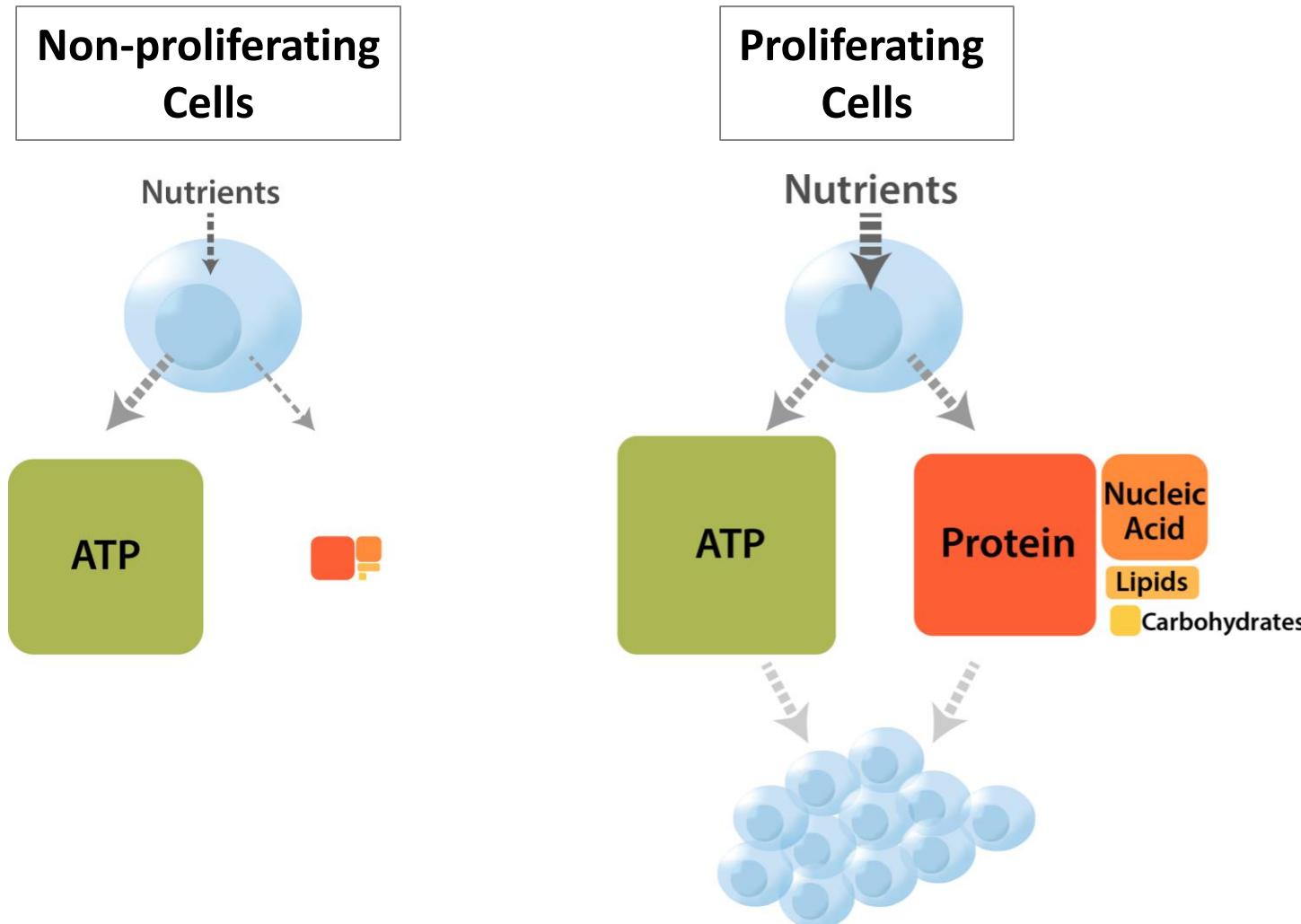
Disclosures

MVH is a consultant and SAB member for
Agios Pharmaceuticals
iTeos Therapeutics
Faeth Therapeutics
Sage Therapeutics
Droia Ventures
Auron Therapeutics

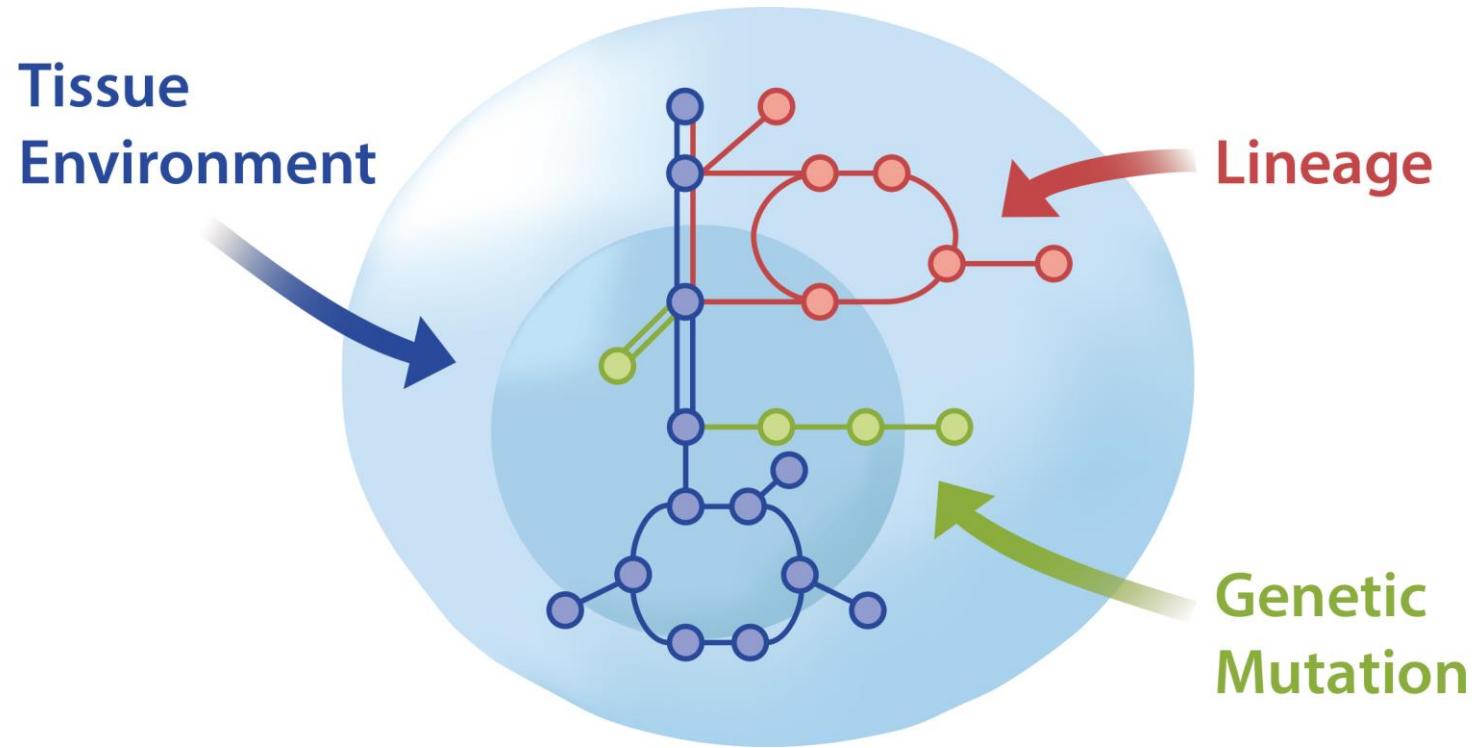
Altered metabolism in cancer involves both cancer cells and immune cells



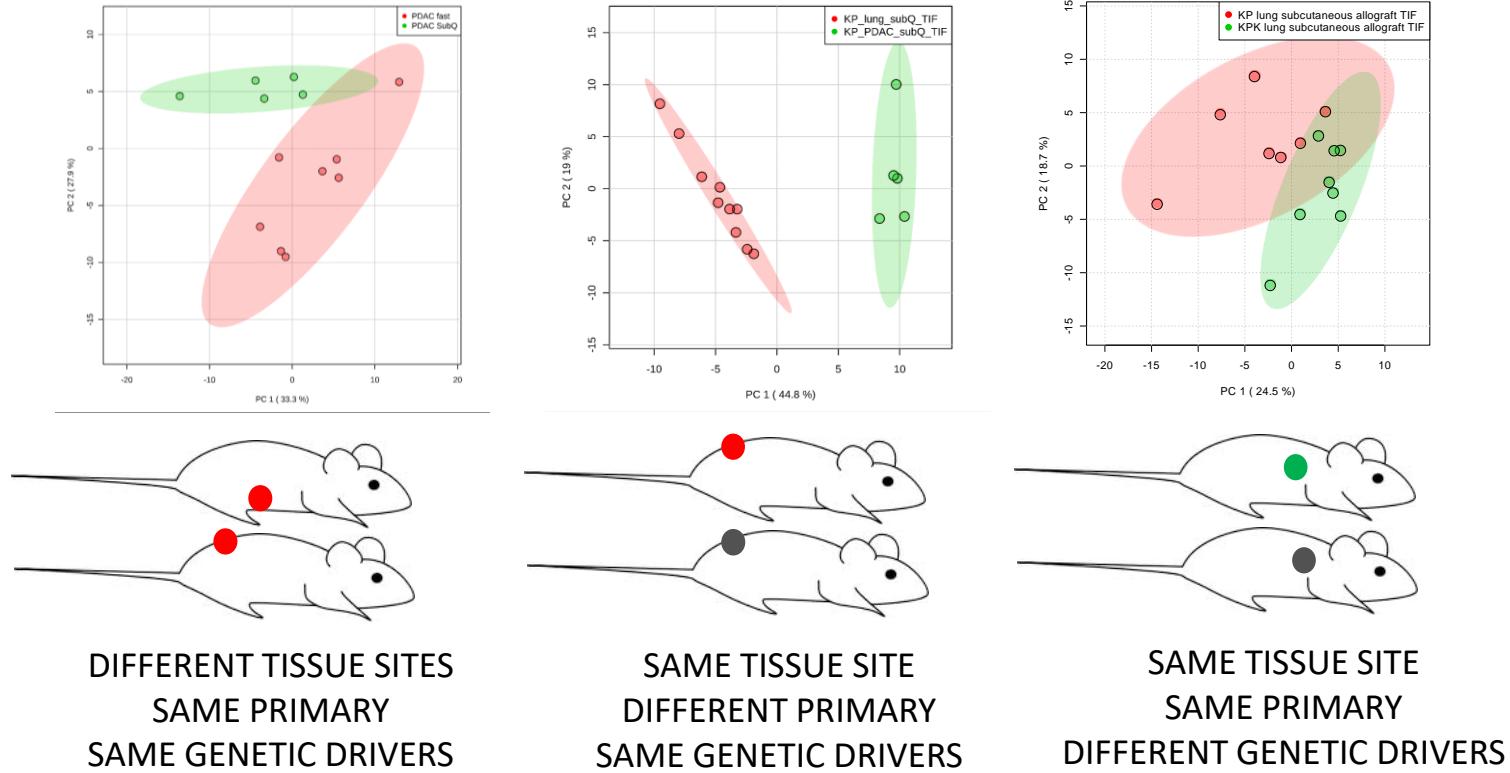
Altered metabolism can reflect how cells adapt to their environment and meet their metabolic demands



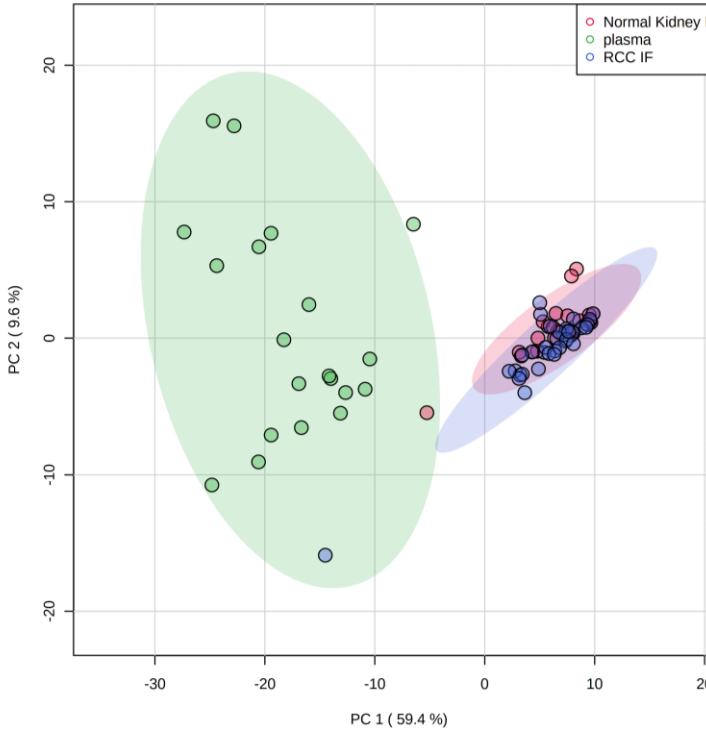
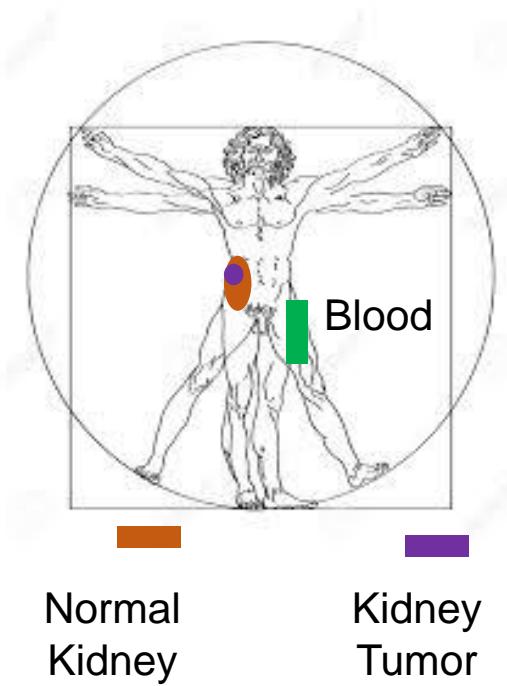
Environment constrains the metabolic network defined by cell intrinsic factors



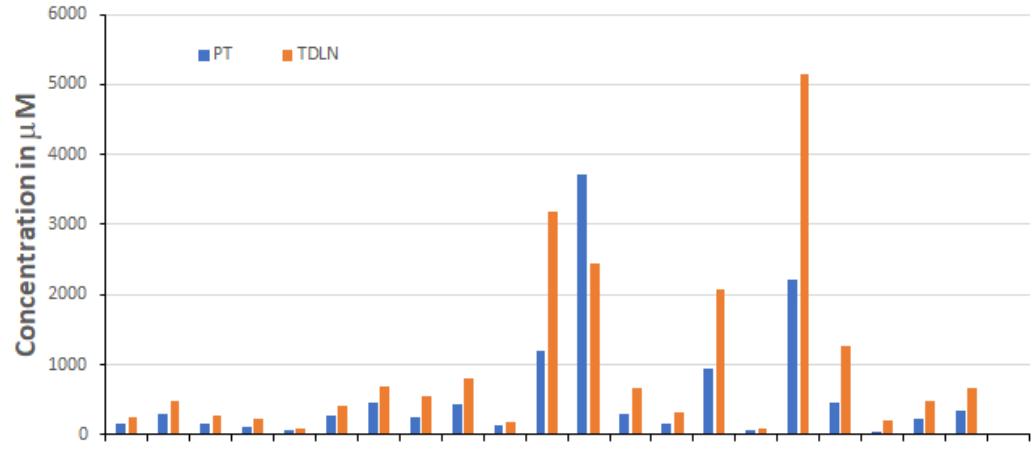
Nutrient availability in tumors varies based on cancer type and tissue location



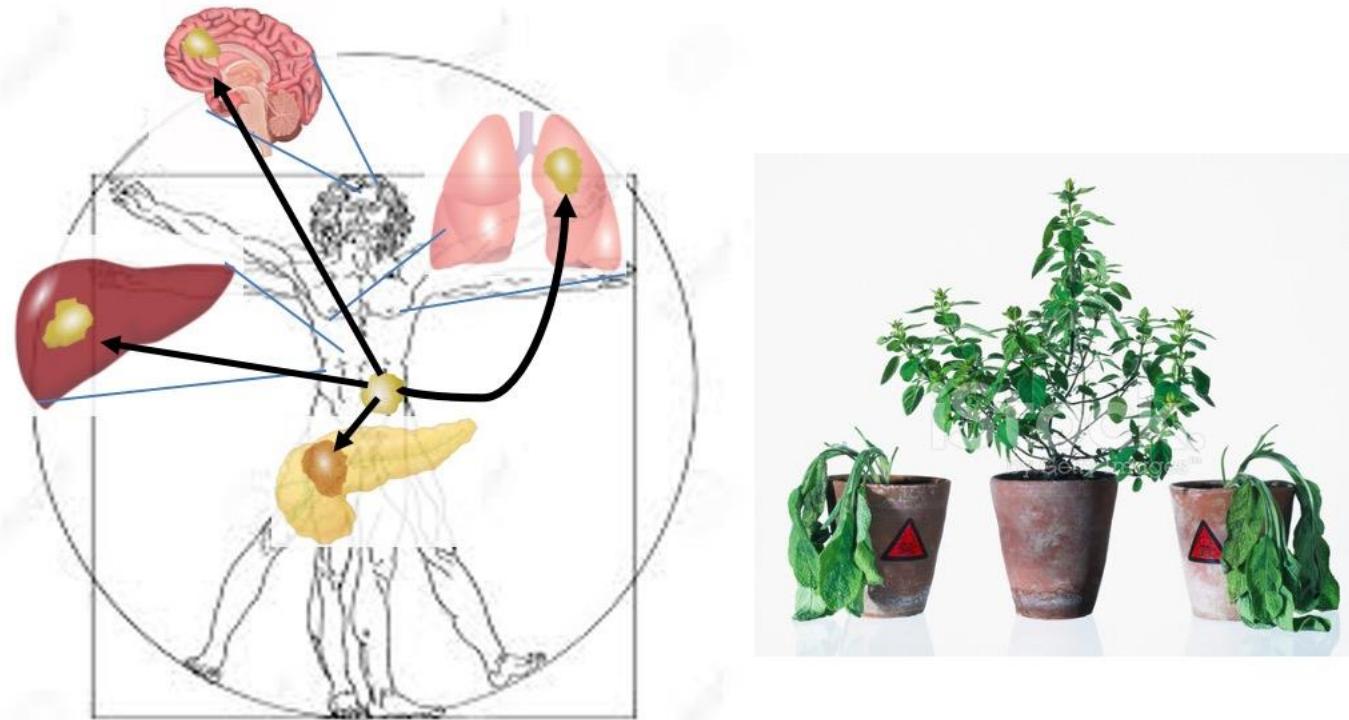
Nutrients found in normal tissues can be similar to those found in tumors



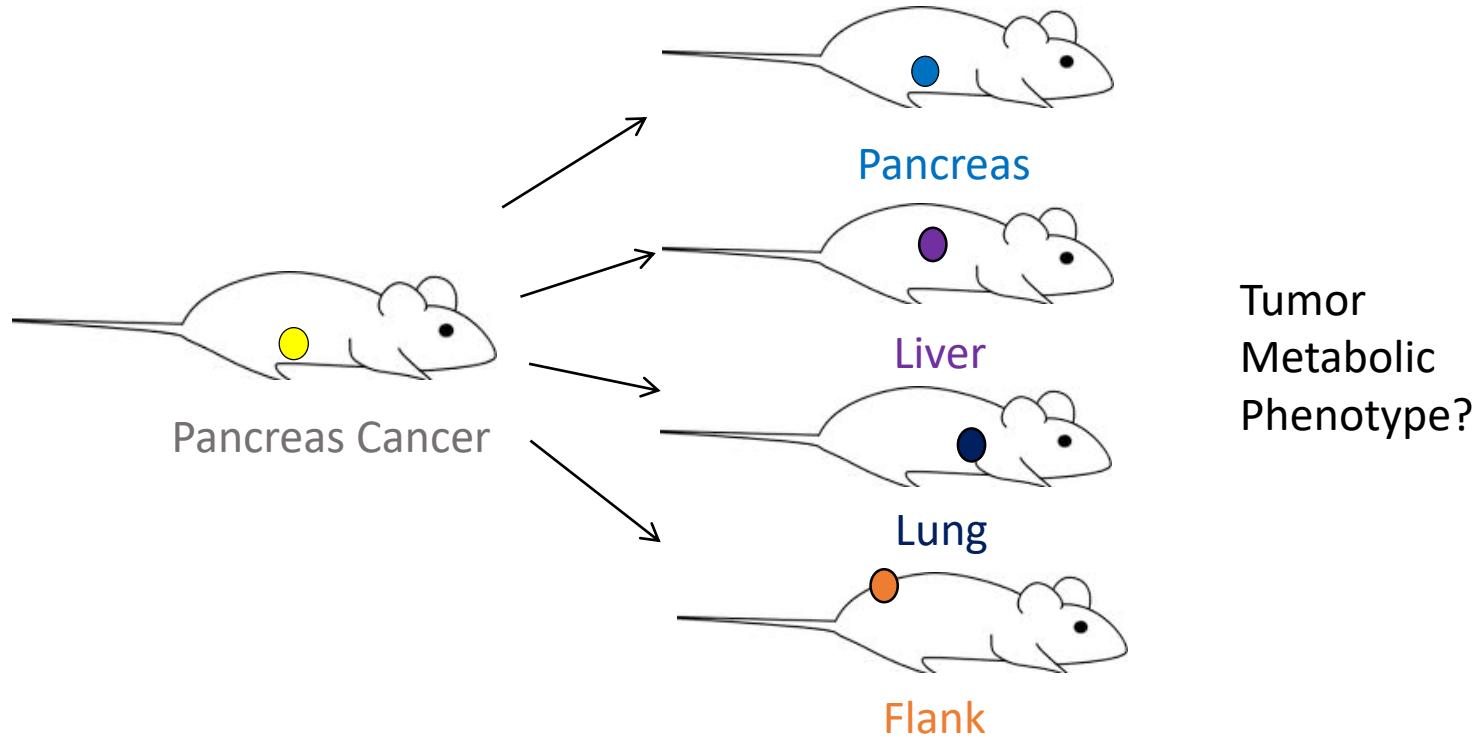
Nutrients available to immune cells in lymph nodes differ from those found in tissues



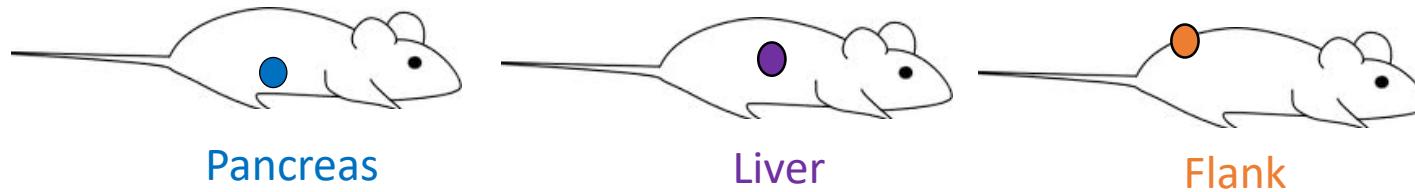
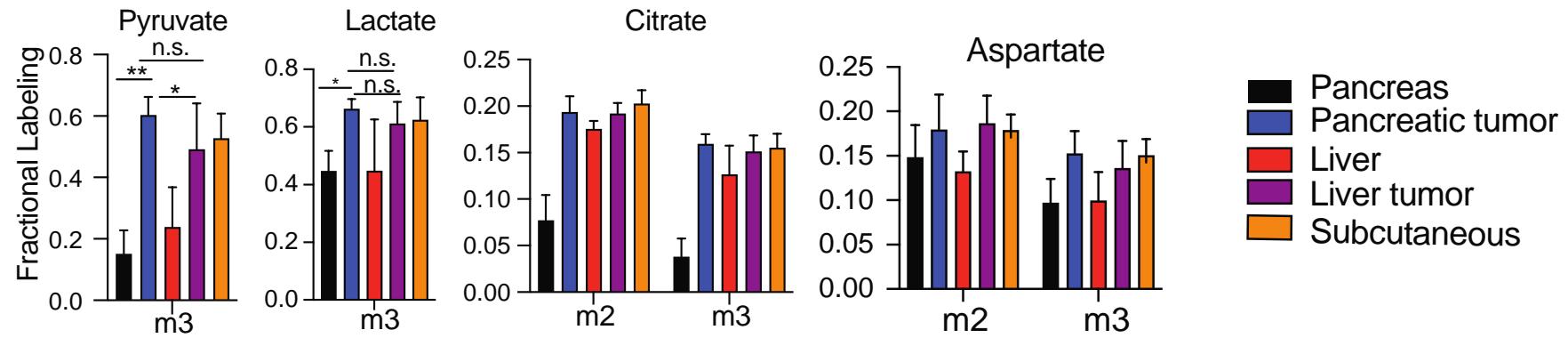
Does tissue nutrient availability restrict where cancer cells form tumors (i.e. metastasis)?



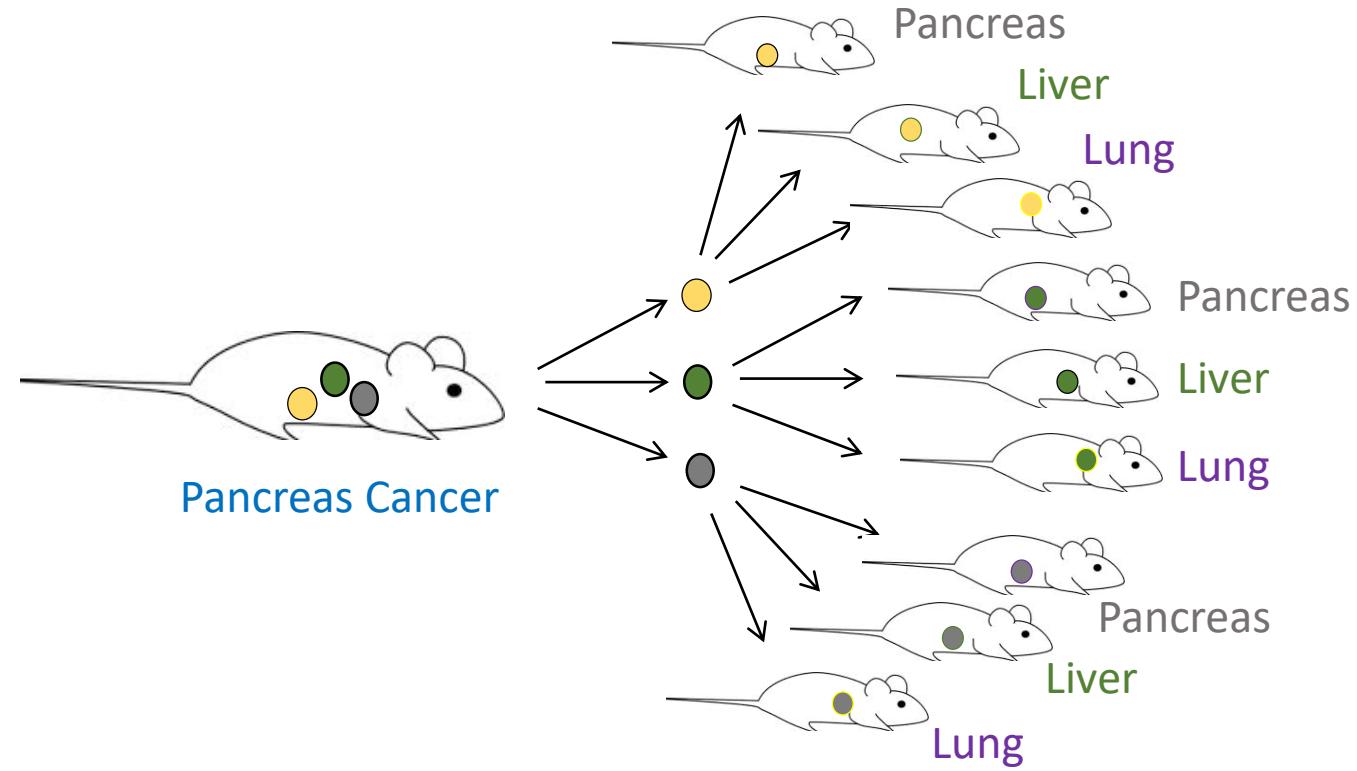
How does tissue site affect tumor metabolism?



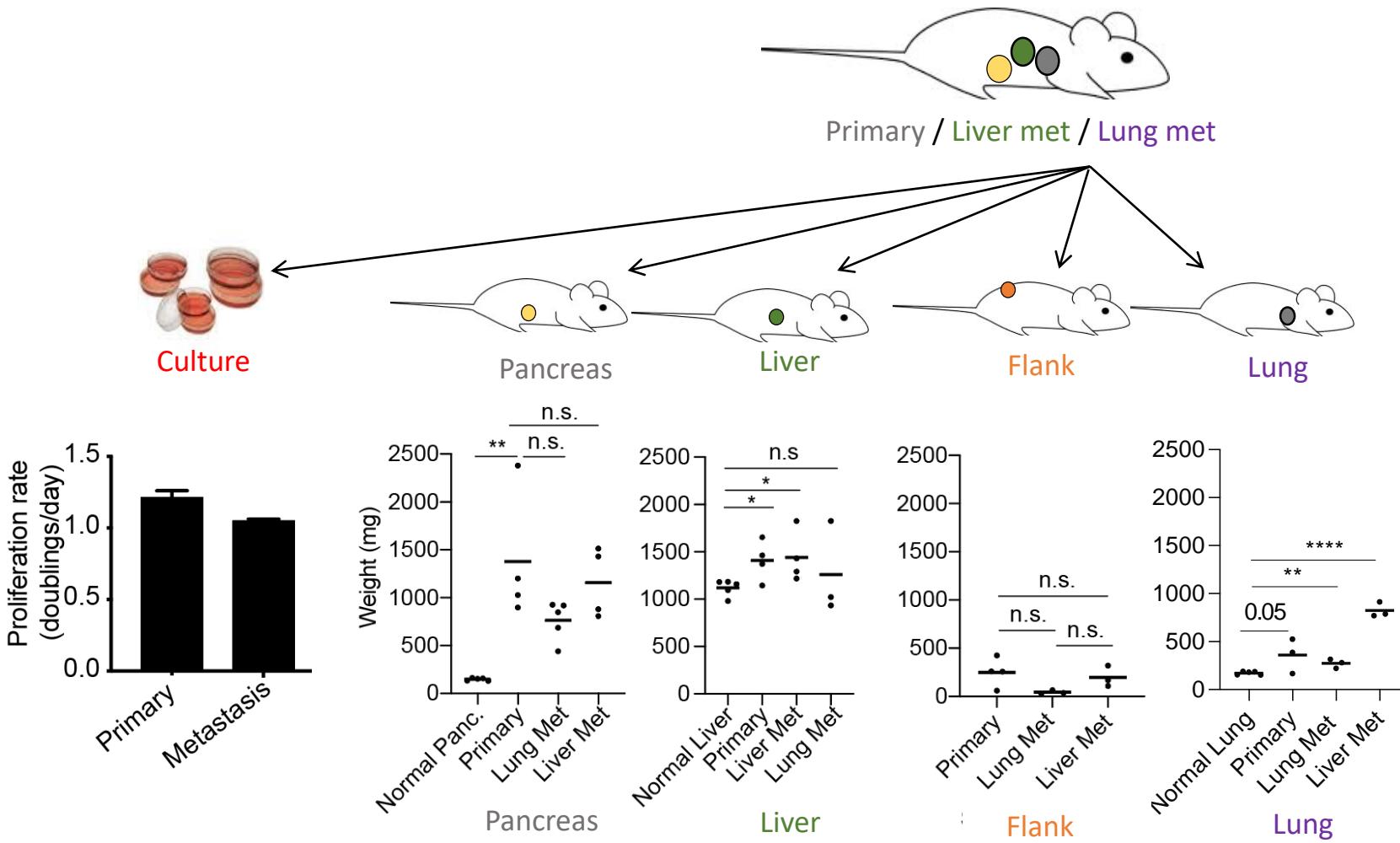
Tumor metabolism is similar in primary tumors and metastases



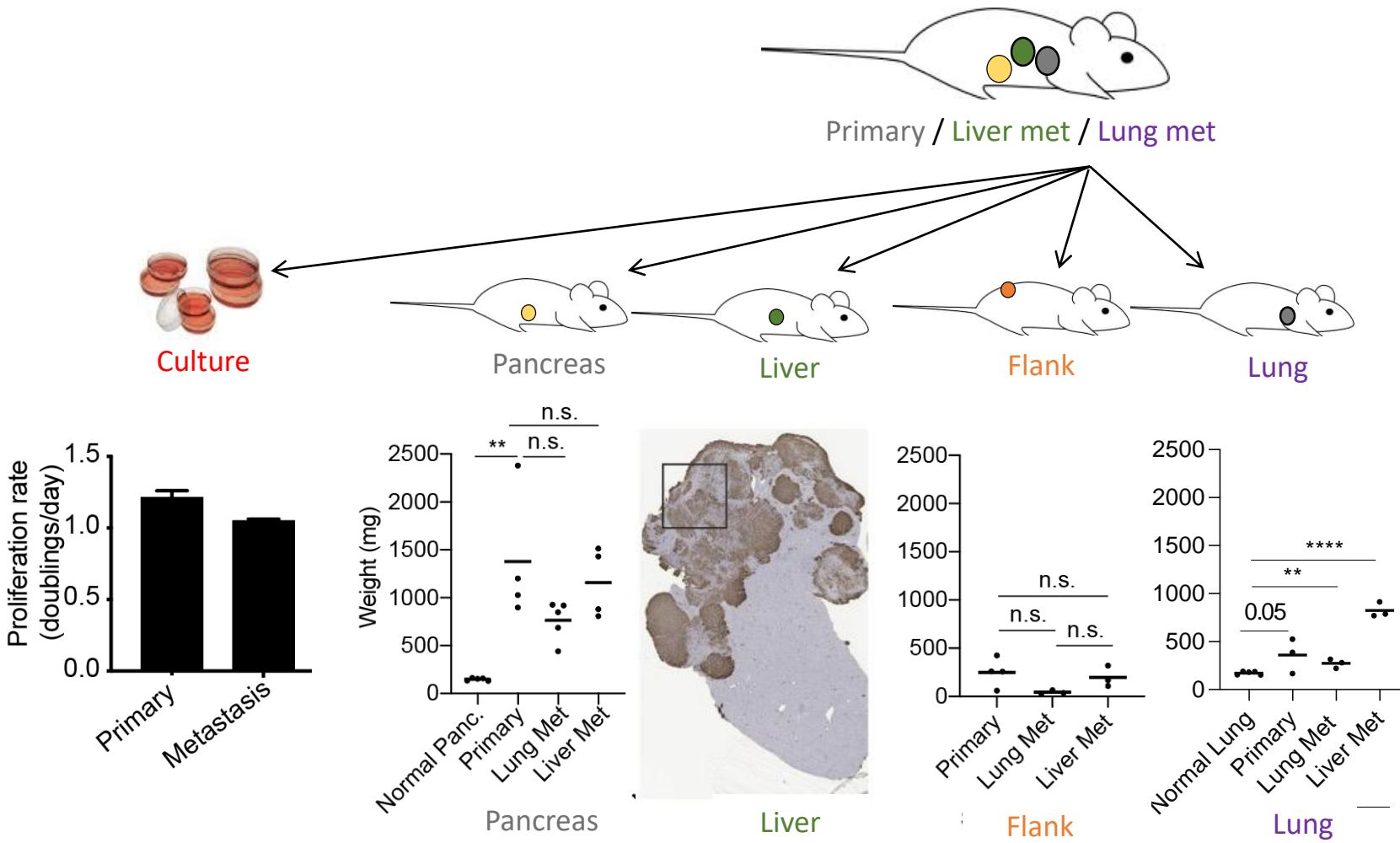
Assessing tissue preference for growth of cancer cells at primary and metastatic sites



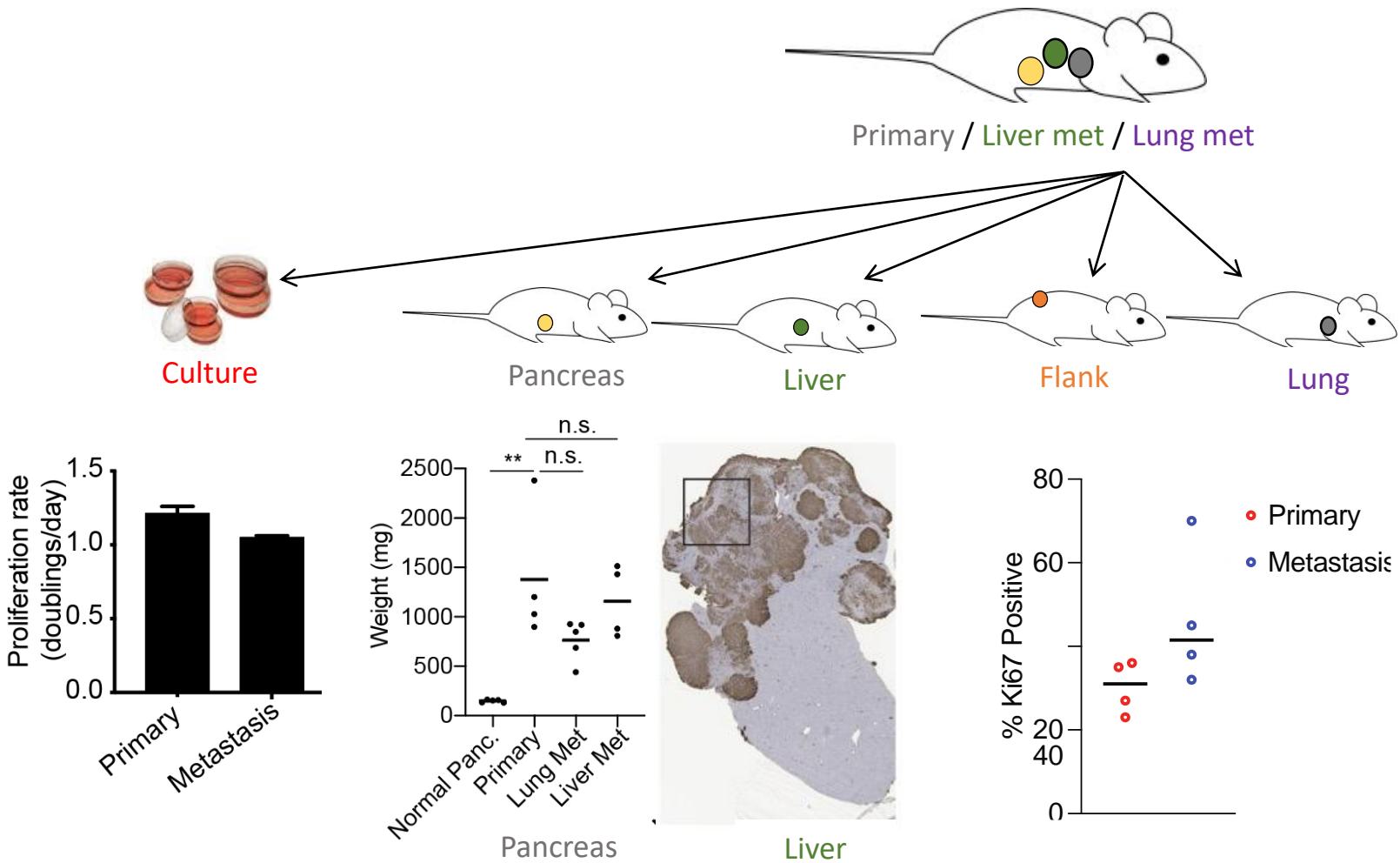
Primary and metastatic PDAC forms tumors in all sites, but grow best in the primary site



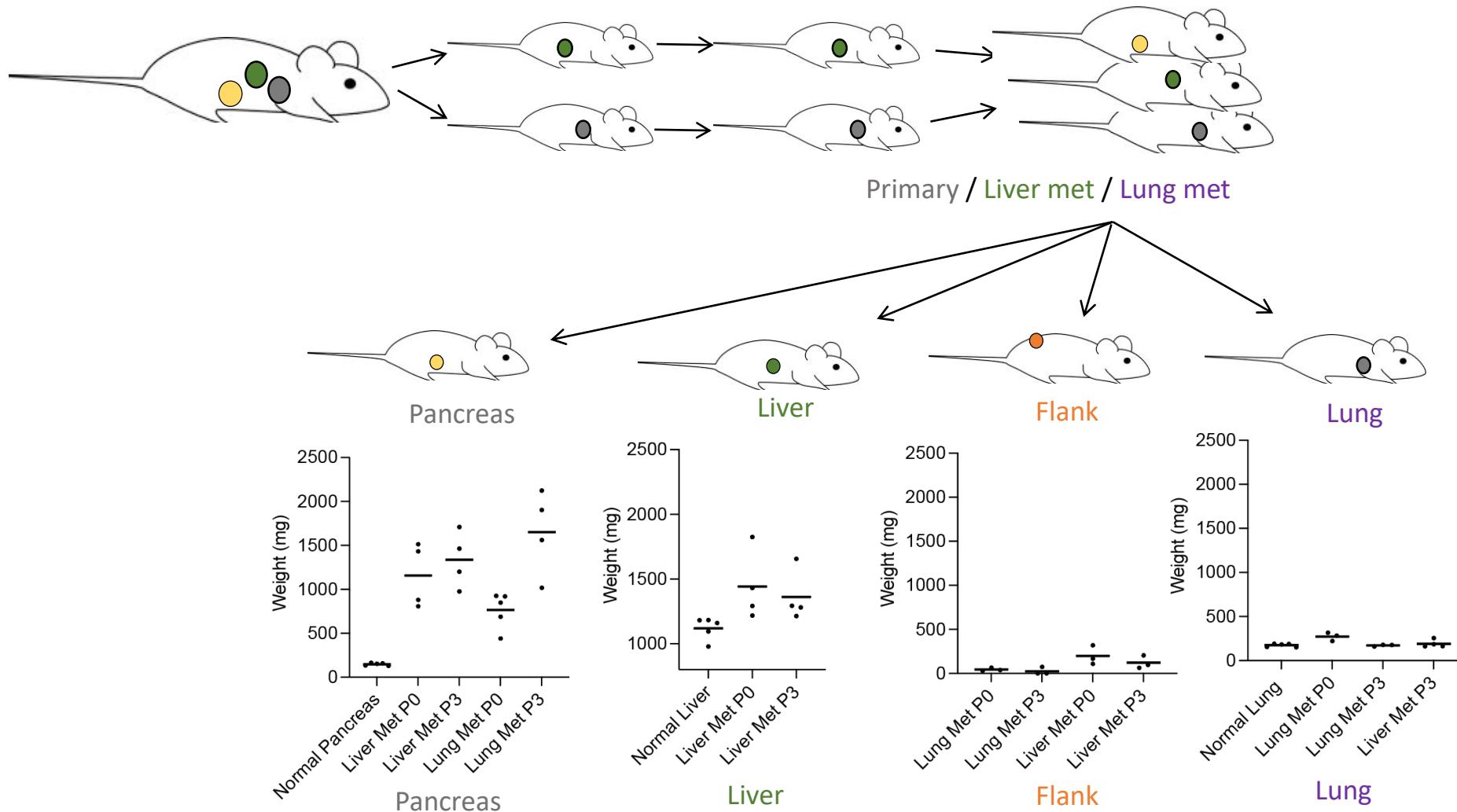
Primary and metastatic PDAC forms tumors in all sites, but grow best in the primary site



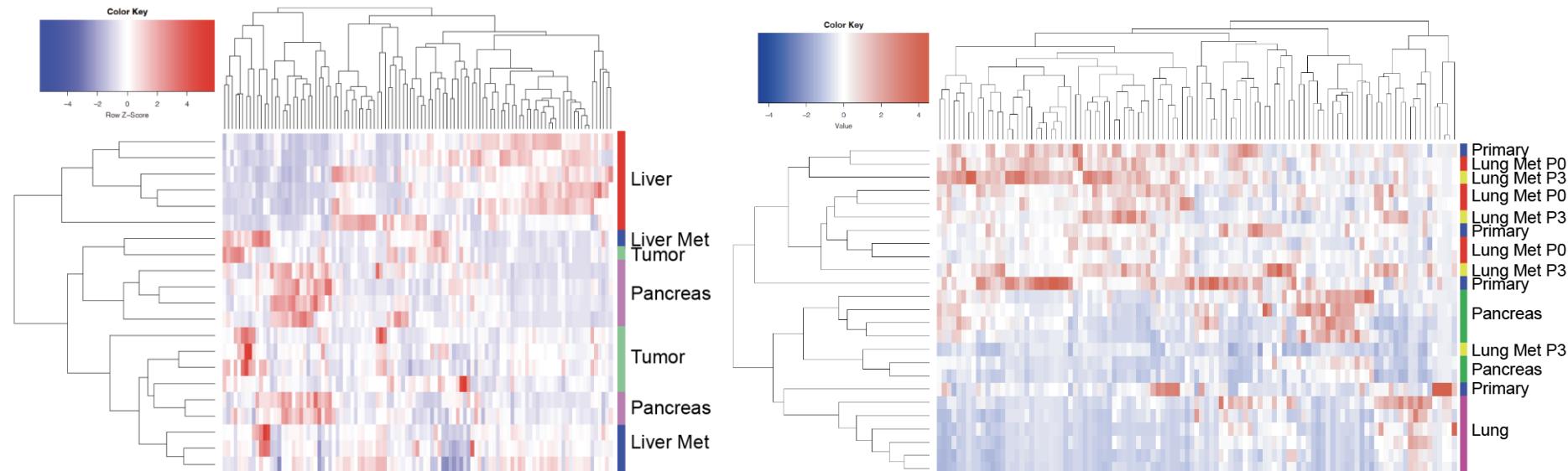
Primary and metastatic PDAC forms tumors in all sites, but grow best in the primary site



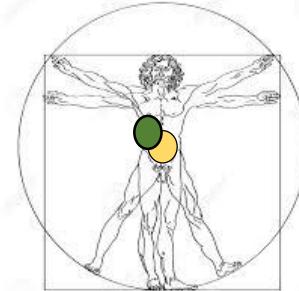
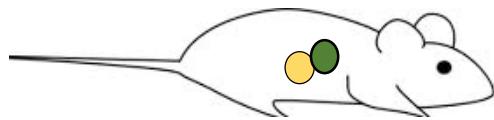
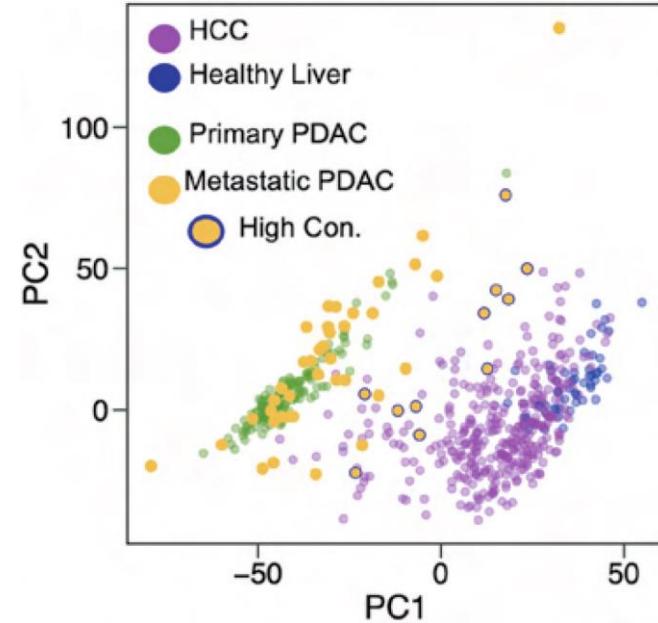
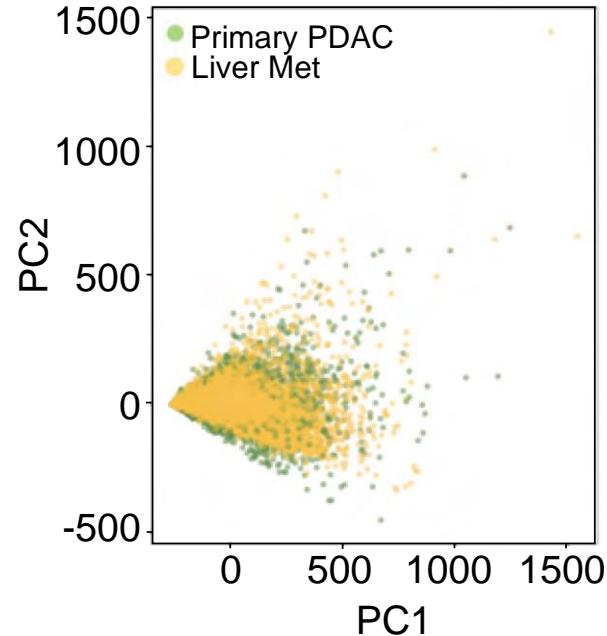
Primary and metastatic PDAC forms tumors in all sites, but grow best in the primary site



Evidence for a similar metabolism in primary and metastatic tumors

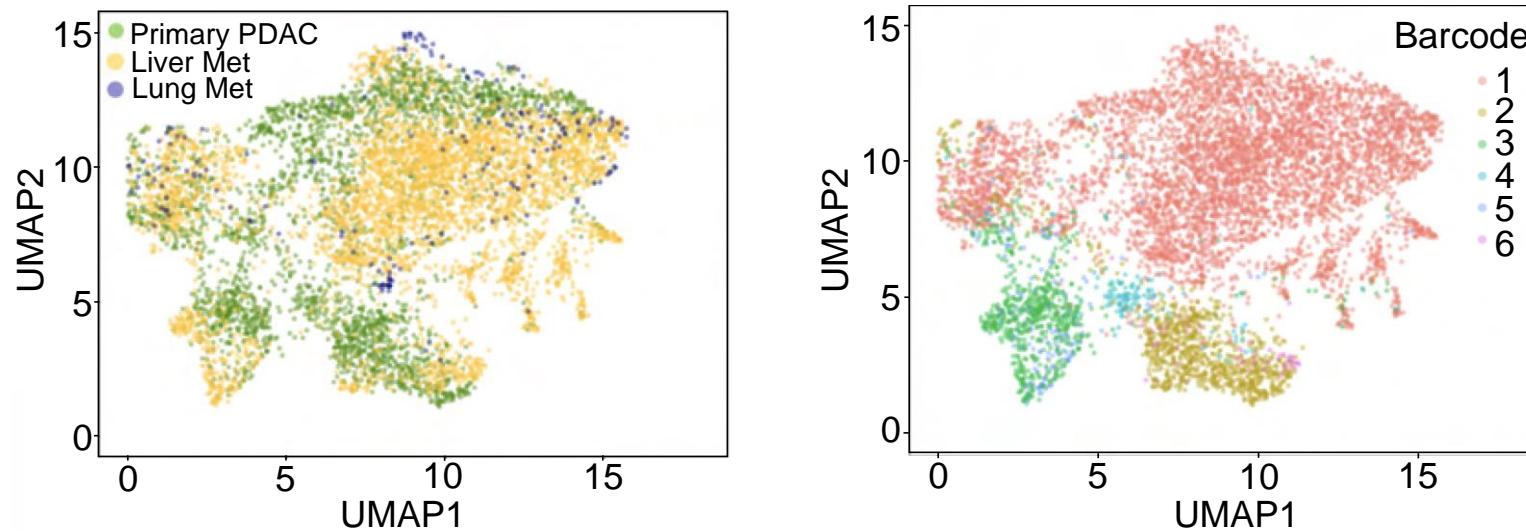


Evidence for a similar metabolism in primary and metastatic tumors

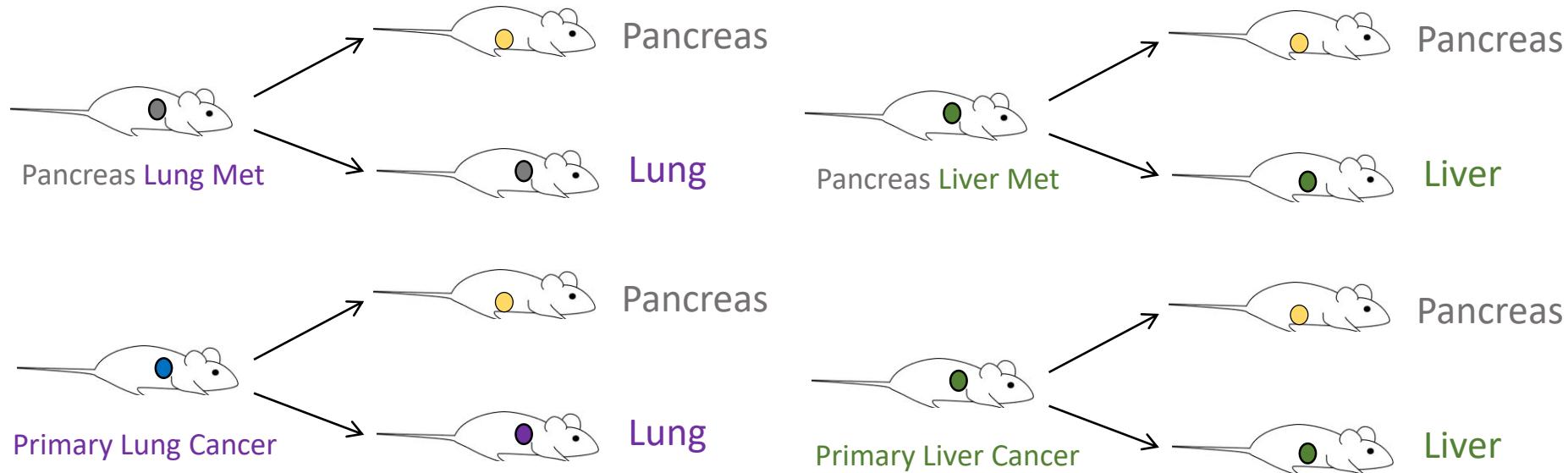


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Sidney Vermeulen
Peter Winter
Alex Shalek
Andy Aguirre

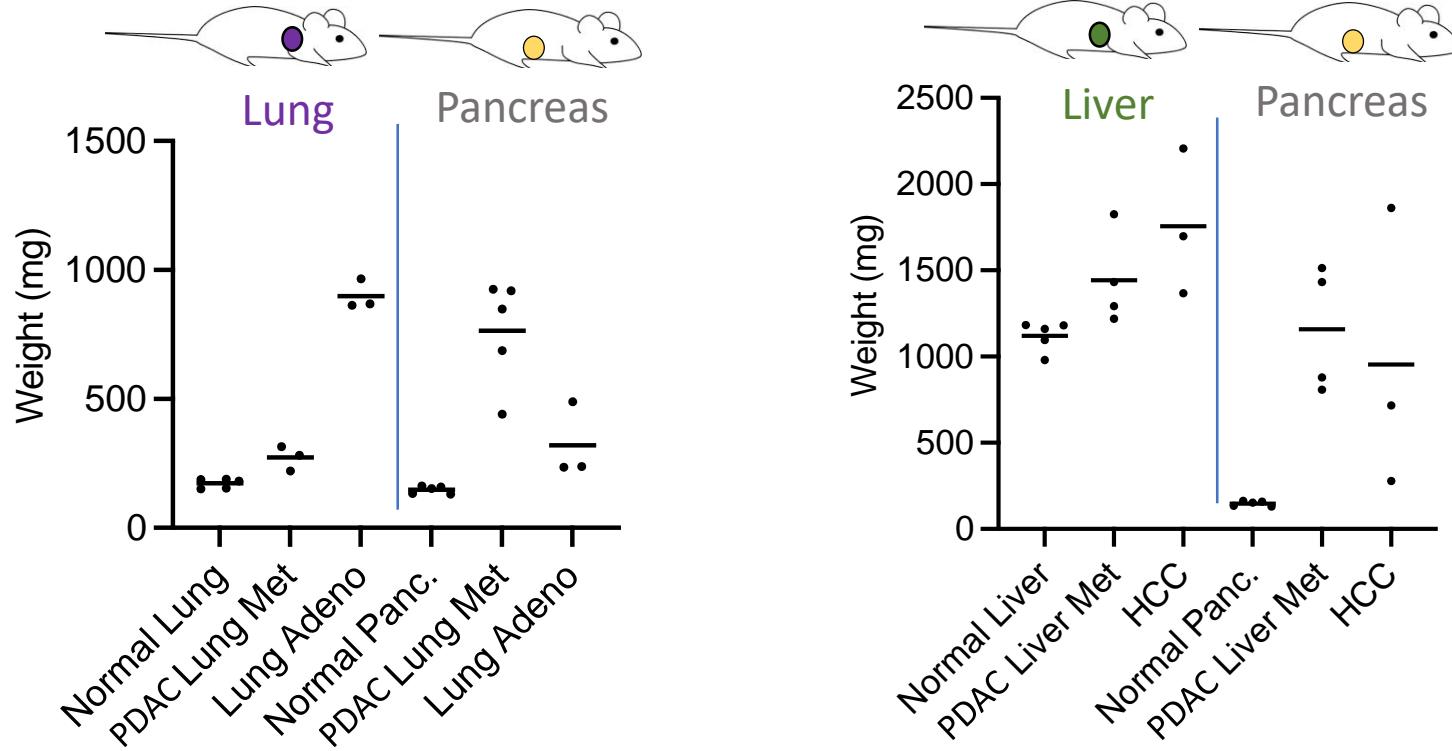
Similar metabolic heterogeneity is observed in primary and metastatic tumors



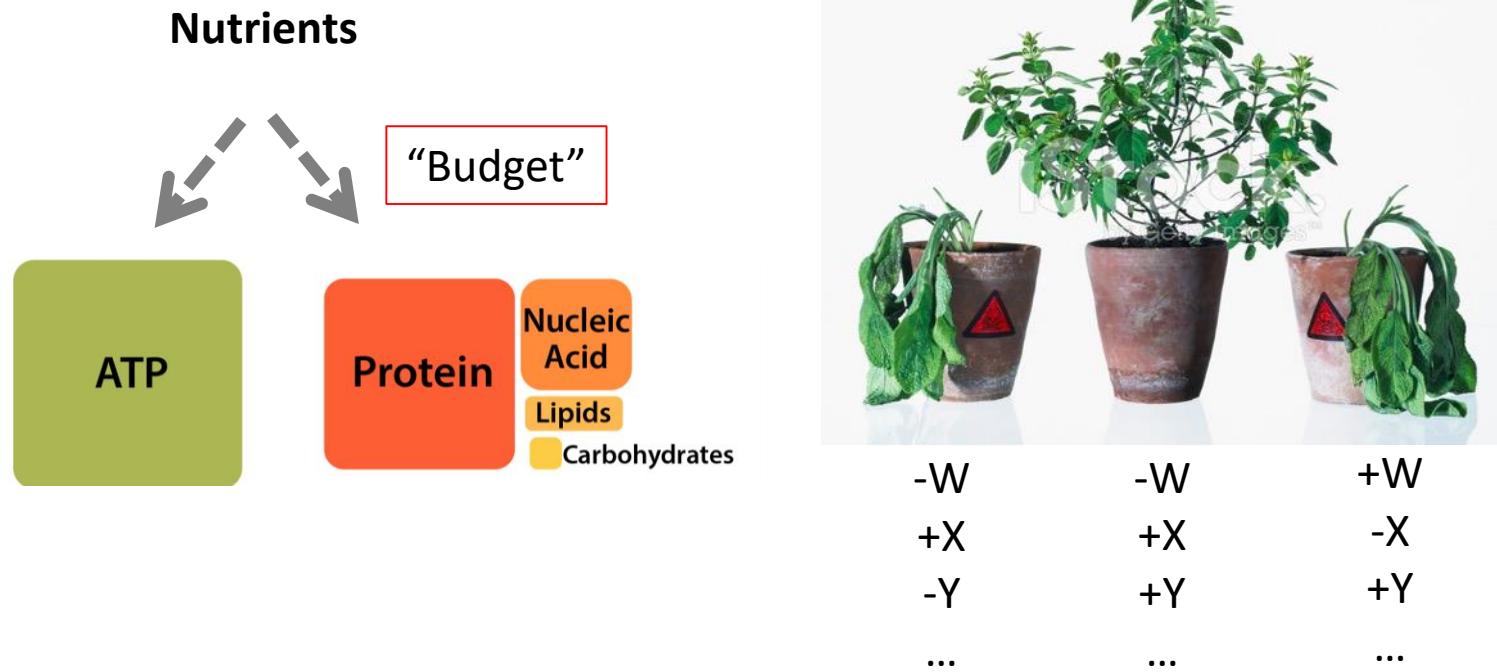
Is accessing the right nutrient environment important for tumor growth?



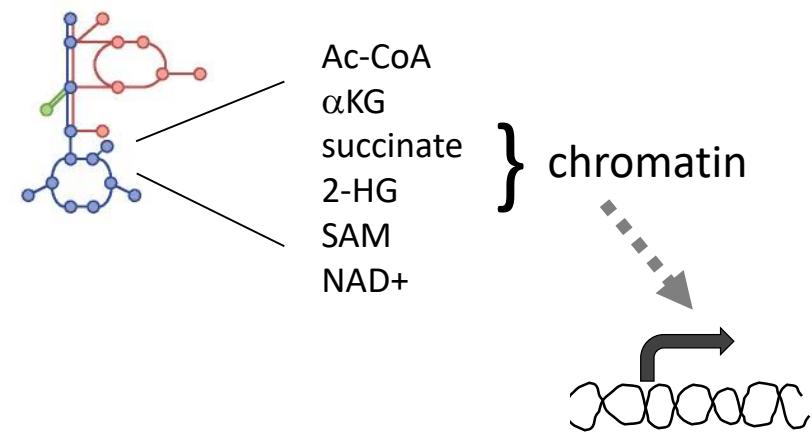
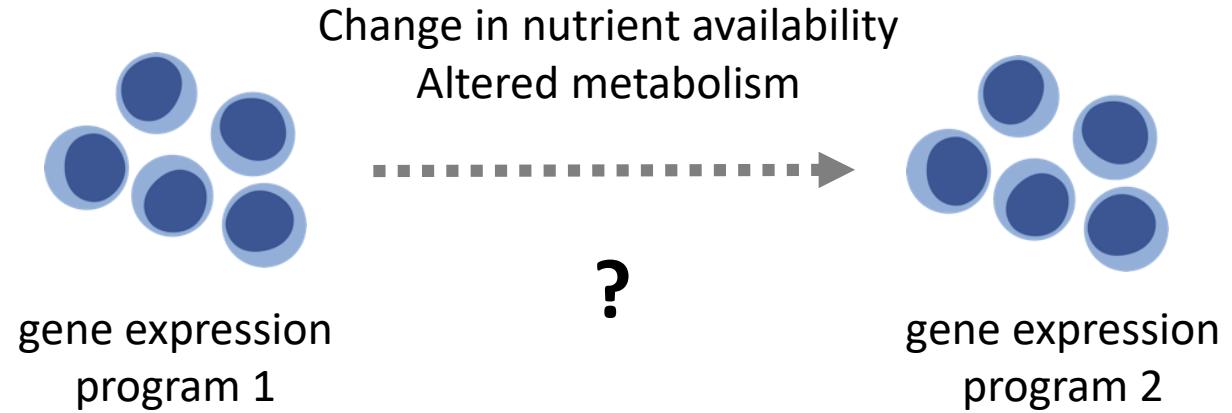
Cancer cells from metastatic tumors grow best in the primary tissue site



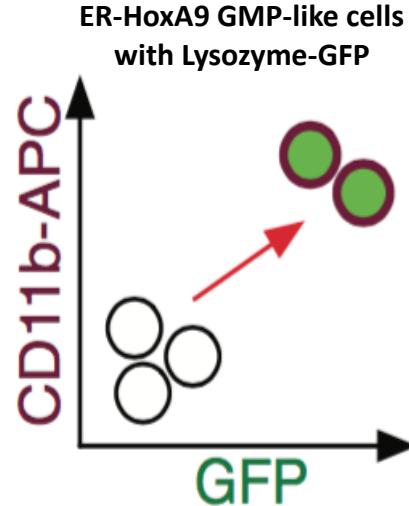
Differentially nutrient availability may impact whether cells can function in different tissues



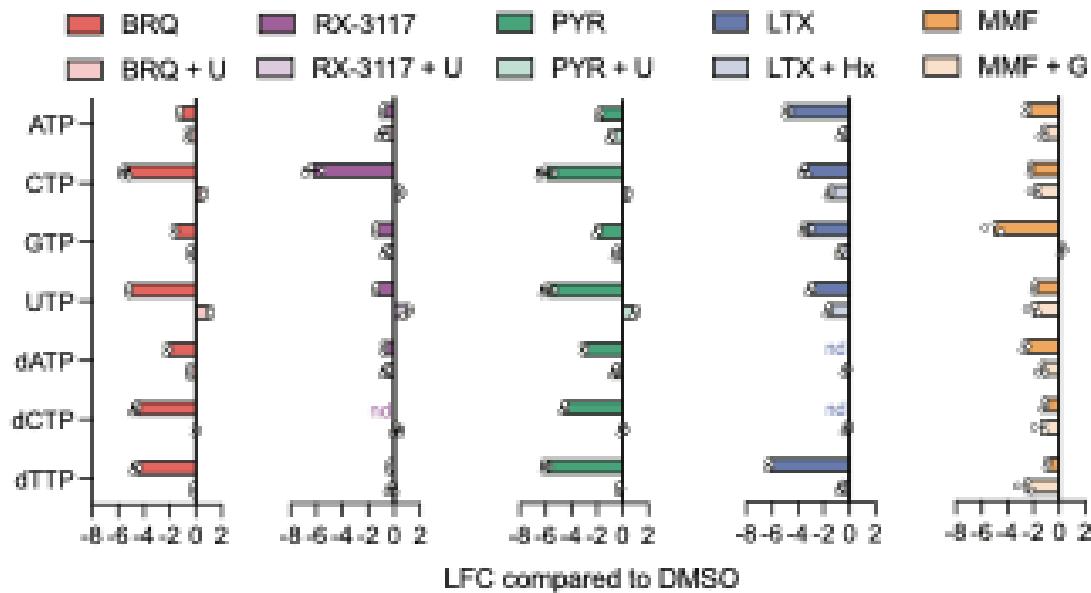
Nutrient use can influence cell state



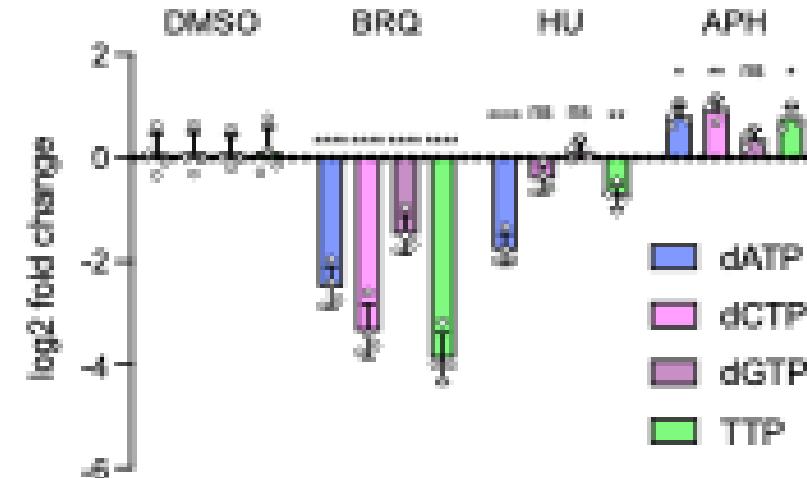
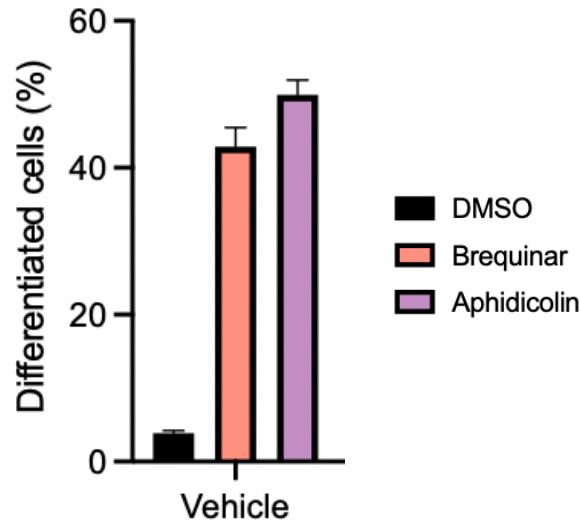
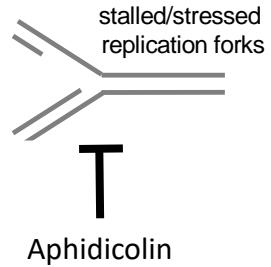
Perturbing levels of one or more nucleotides can promote hematopoietic cell differentiation



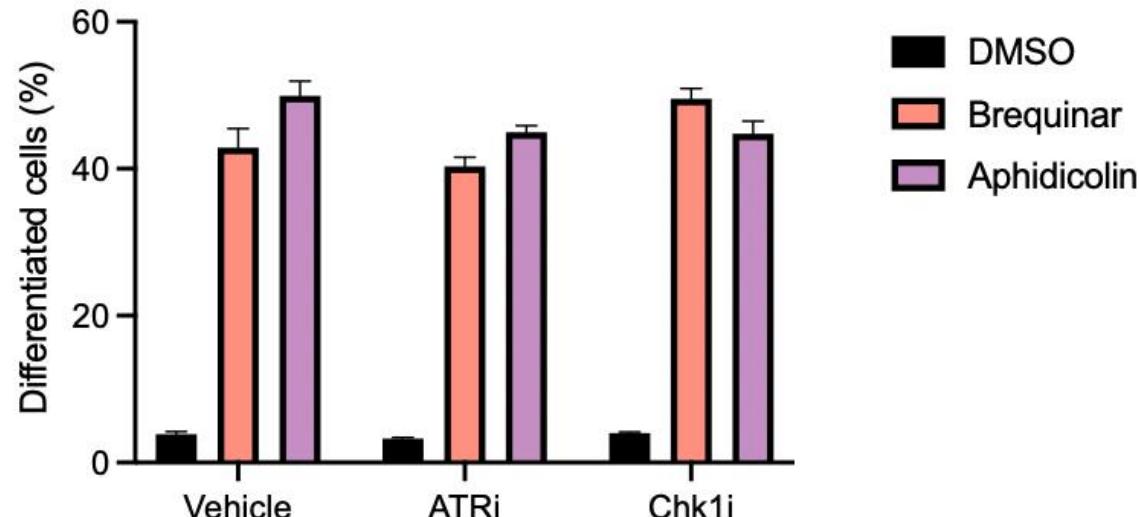
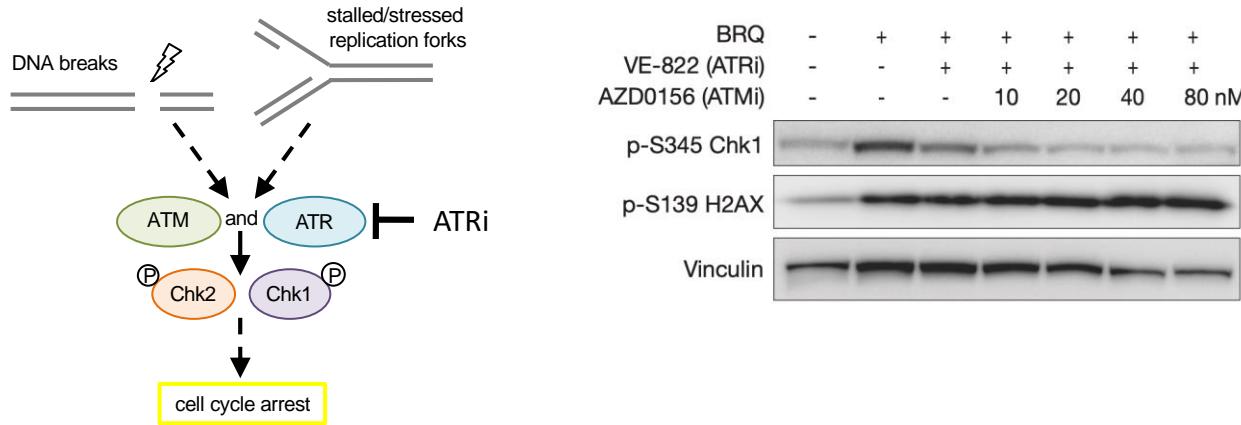
Sykes et al. Cell 2016.



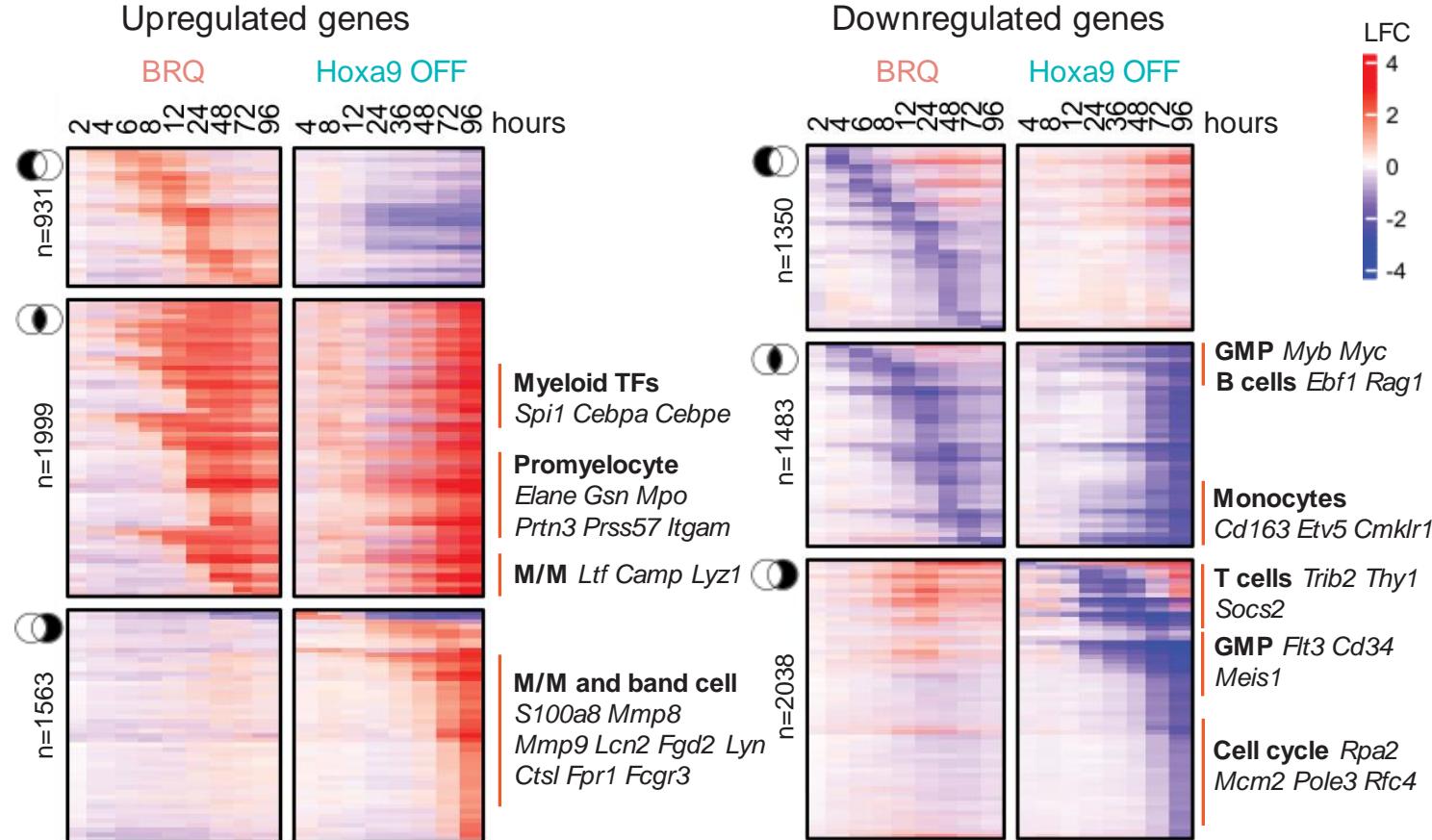
Replication stress can promote cell state changes downstream of altered nucleotide levels



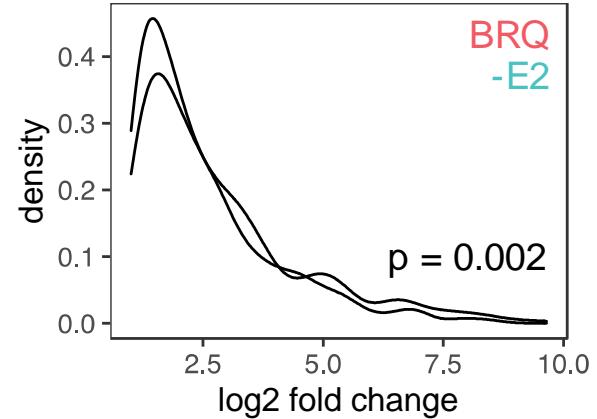
Replication stress affects on cell state do not require replication stress signaling



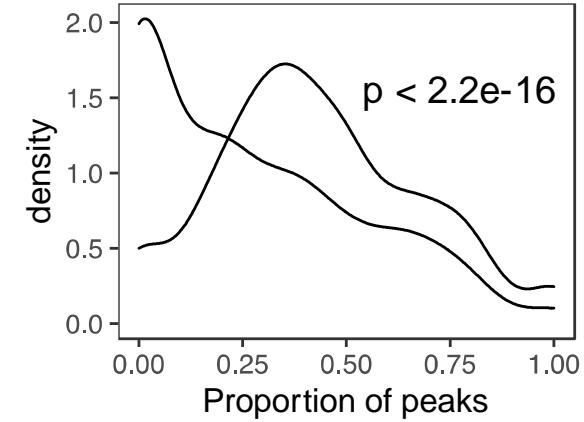
Replication stress impacts expression of some lineage specific genes



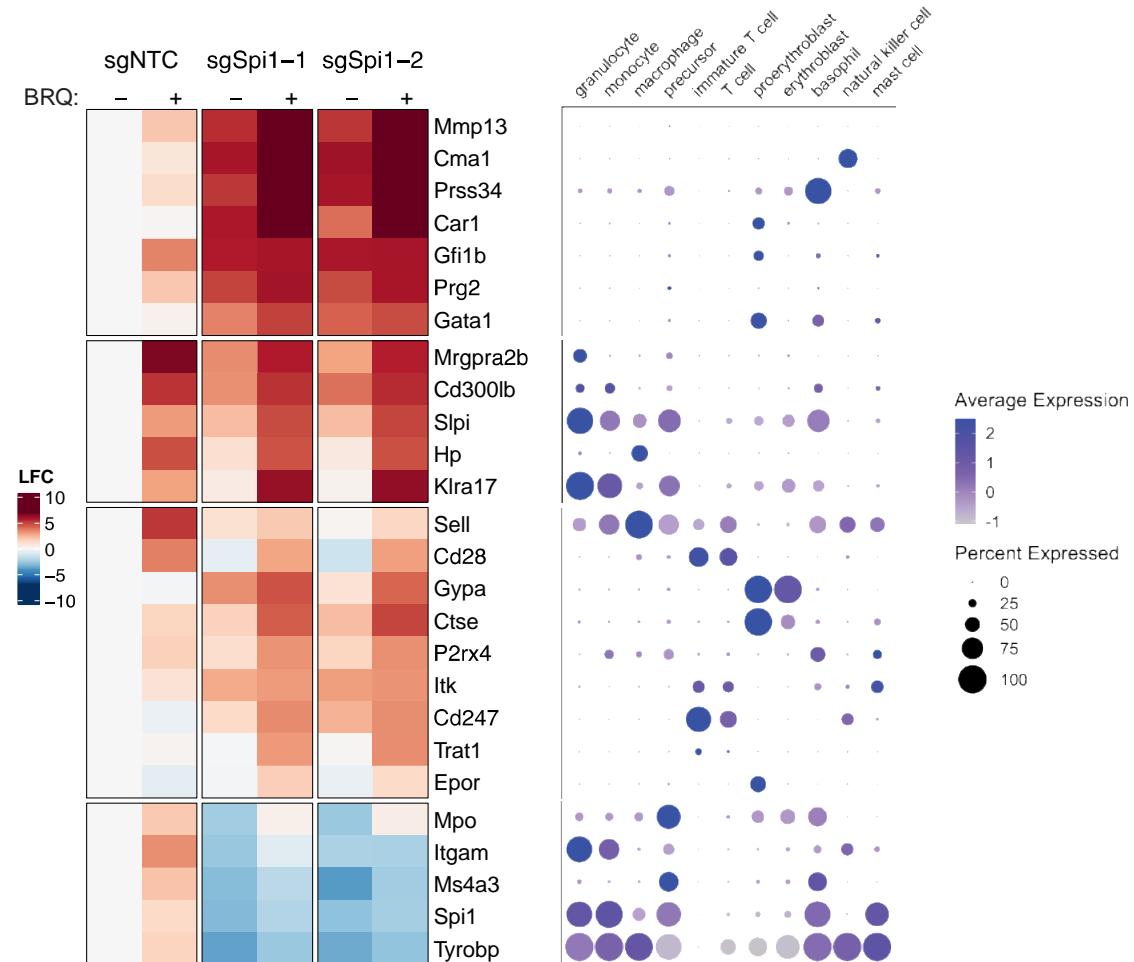
Change in expression for shared upregulated genes



Proportion of peaks that gain accessibility



Replication stress promotes progression along a cell state trajectory that is dependent on TF expression



Acknowledgements

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