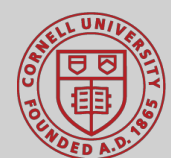


Cornell Center on the Physics of Cancer Metabolism

Claudia Fischbach-Teschl, Meinig School of Biomedical Engineering, Ithaca
Lew Cantley, Meyer Cancer Center, New York

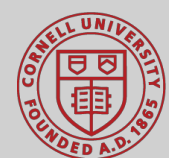
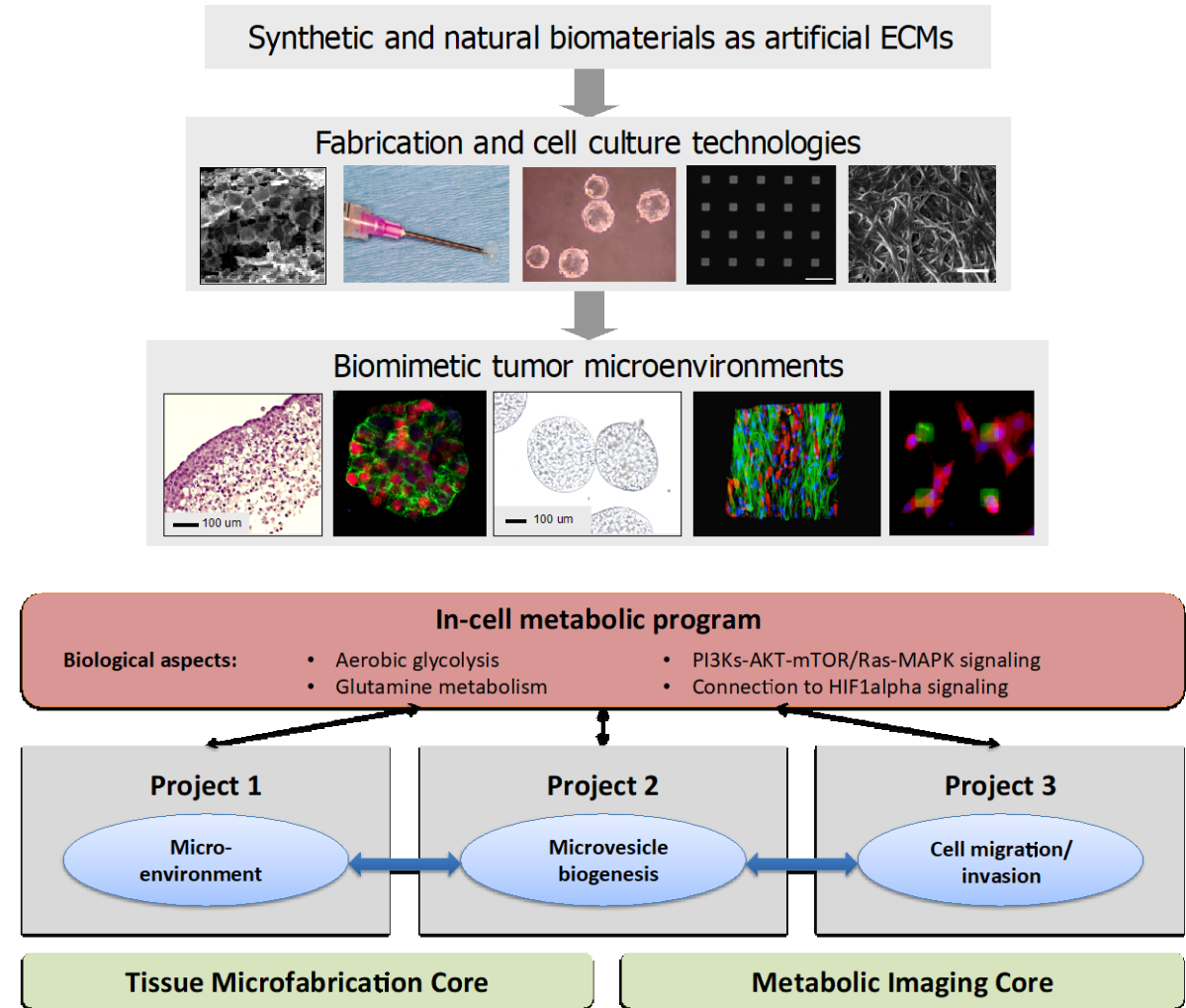
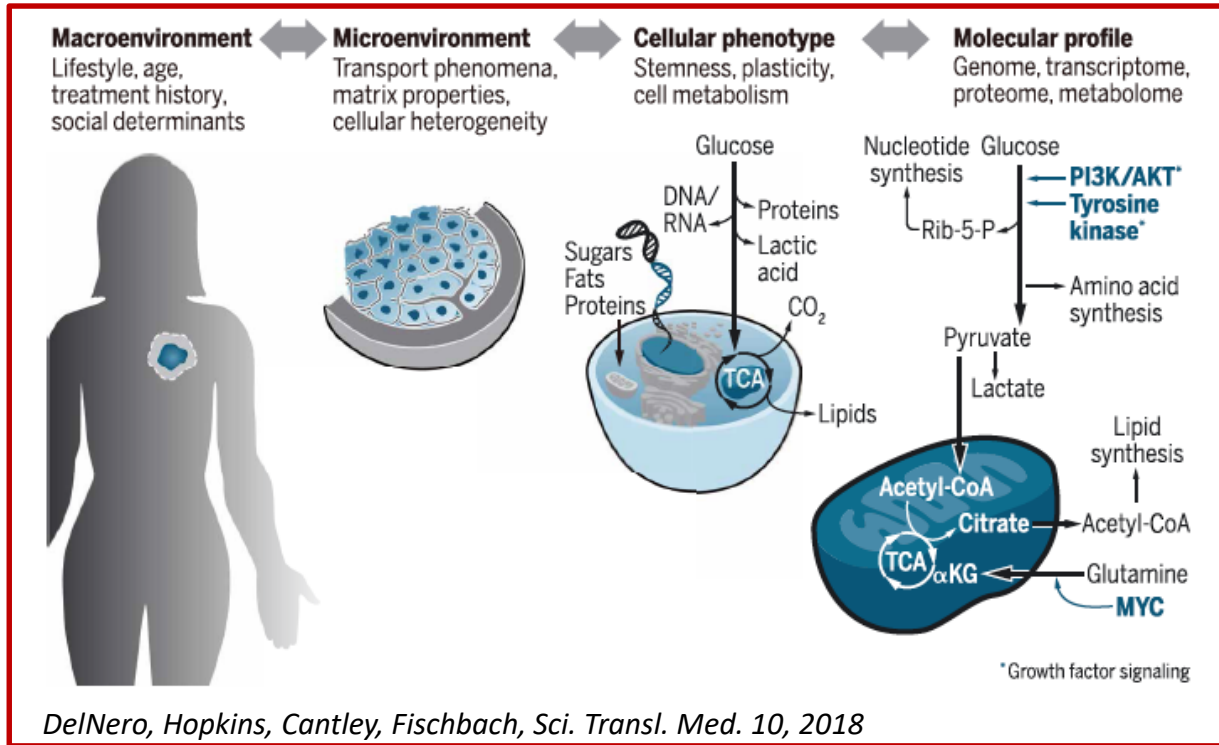
<http://psoc.engineering.cornell.edu>



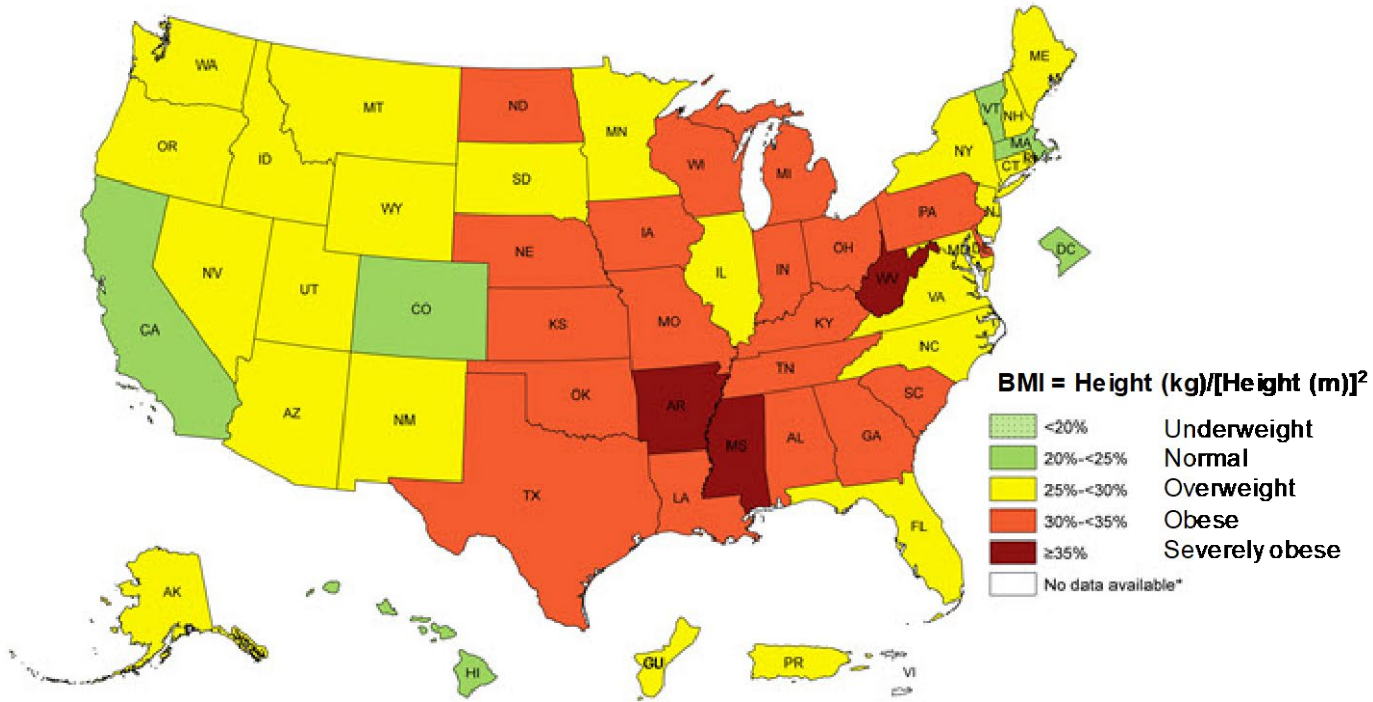
CornellPSOC
Physics of Cancer Metabolism

 **Weill Cornell Medicine**
Sandra and Edward
Meyer Cancer Center

Organizing framework of Cornell PSOC

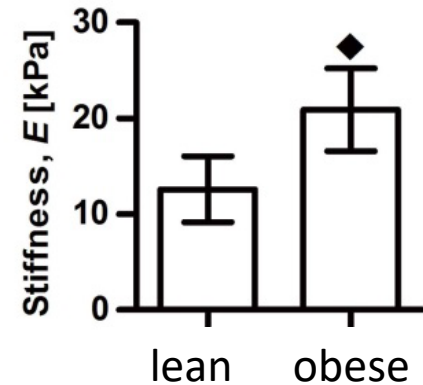
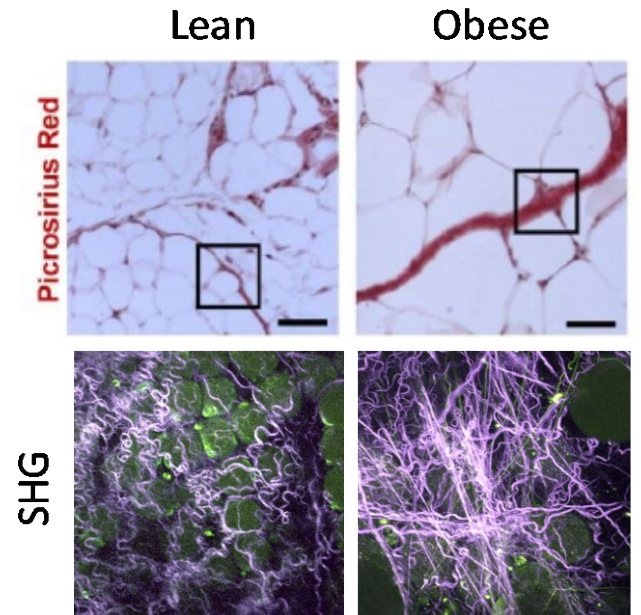


Obesity and Cancer



Center for Disease Control and Prevention (CDC), 2014 and OECD

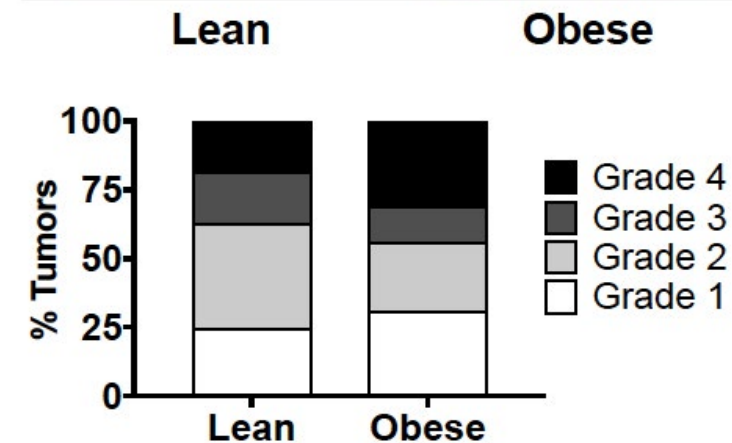
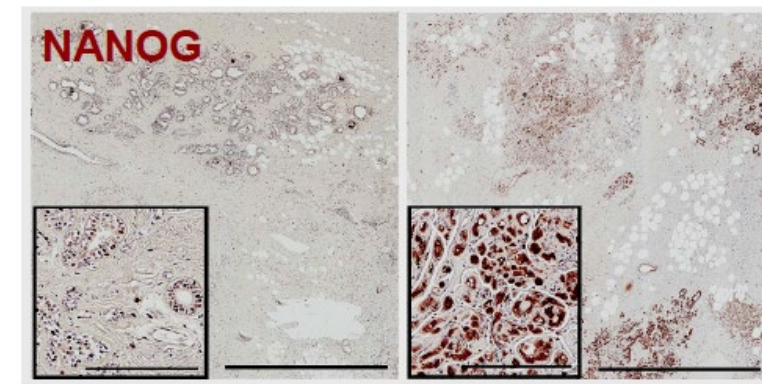
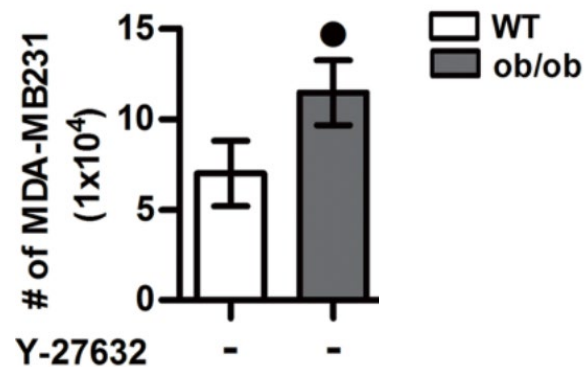
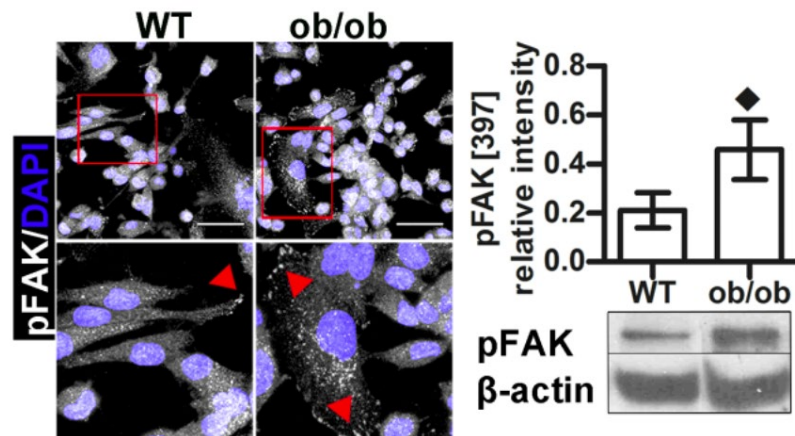
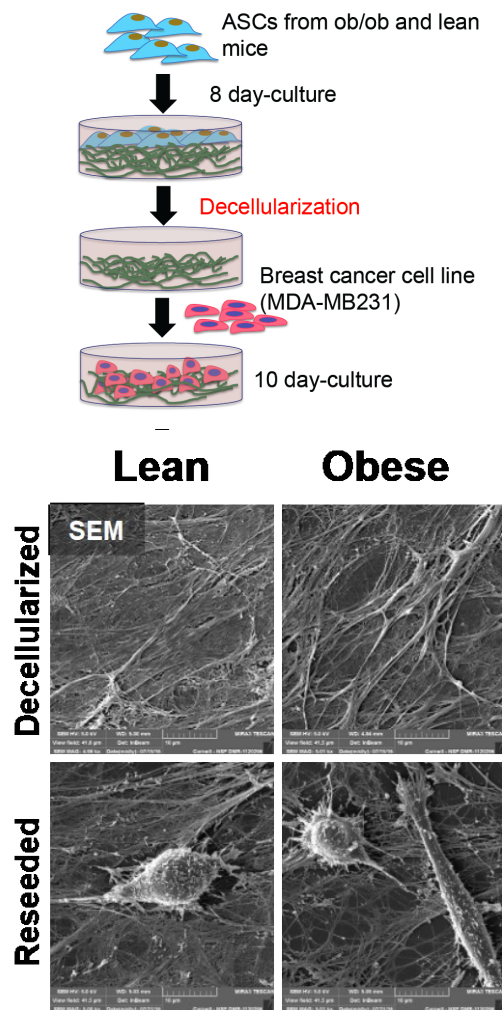
- More than one-third of US adults are obese.
- Obesity is associated with increased risk for cancer and worse prognosis.



Seo B. et al., Science Translational Medicine 2015

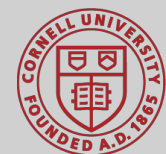


Obesity-associated ECM stimulates breast cancer malignancy in a mechanoresponsive manner

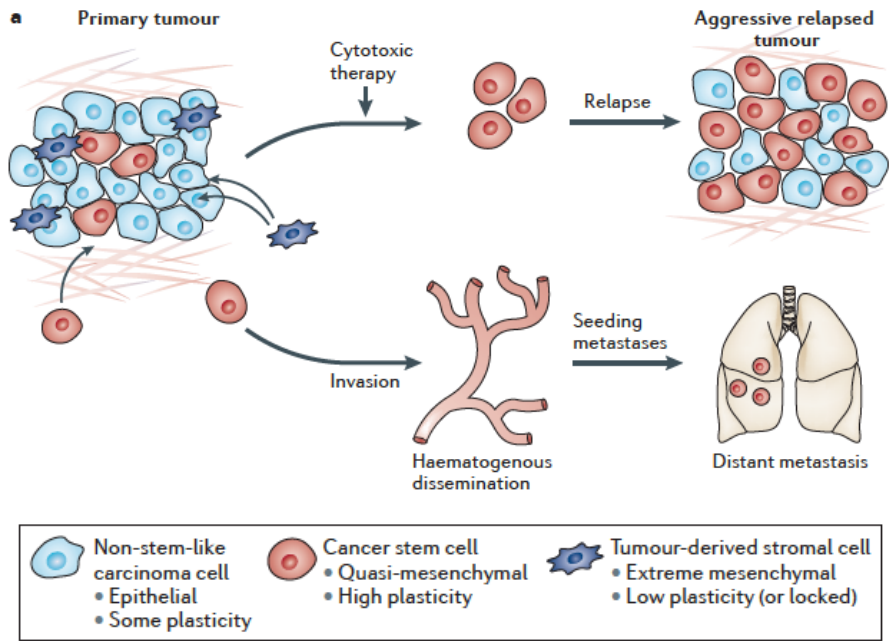


Seo B. et al., Science Translational Medicine 2015

Wittmann K et al., under revision

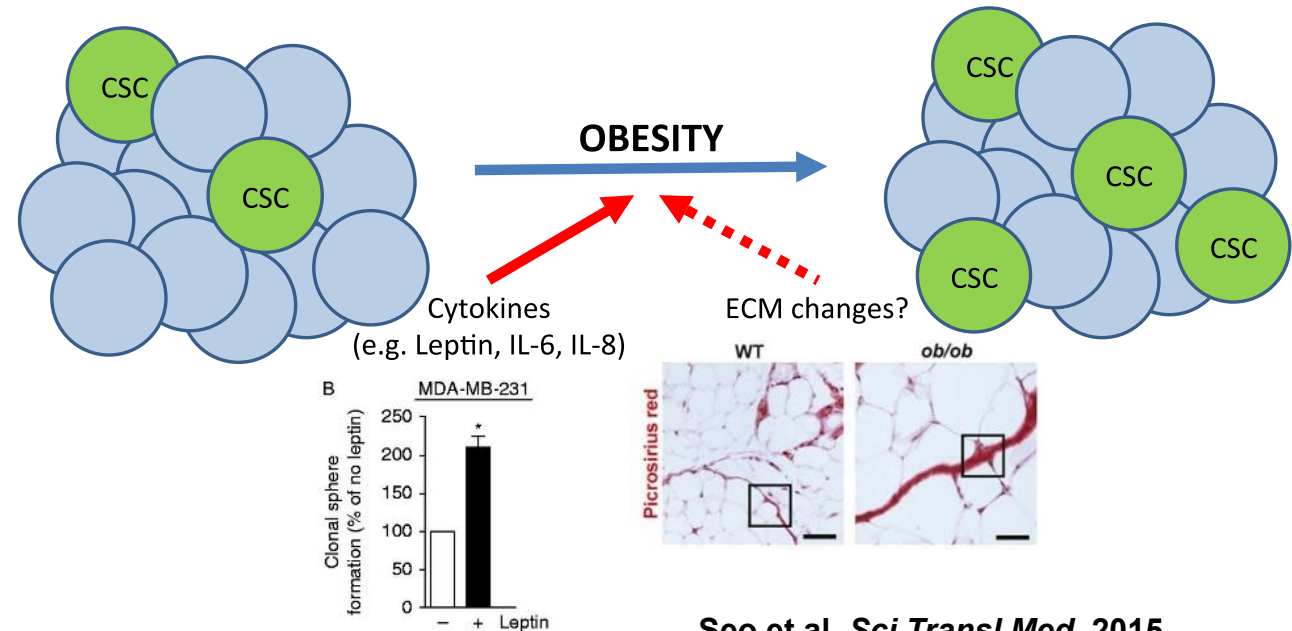


Does obesity-associated ECM affect cancer stem cells (CSCs)?



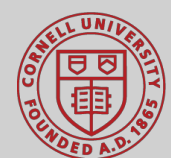
Pattabiraman & Weinberg, *Nat. Reviews Drug Discovery* (2014)

- Expression of stem cell markers (NANOG, SOX2, OCT4, ALDH)
- Self-renewal capabilities
- Therapy resistance and metastasis

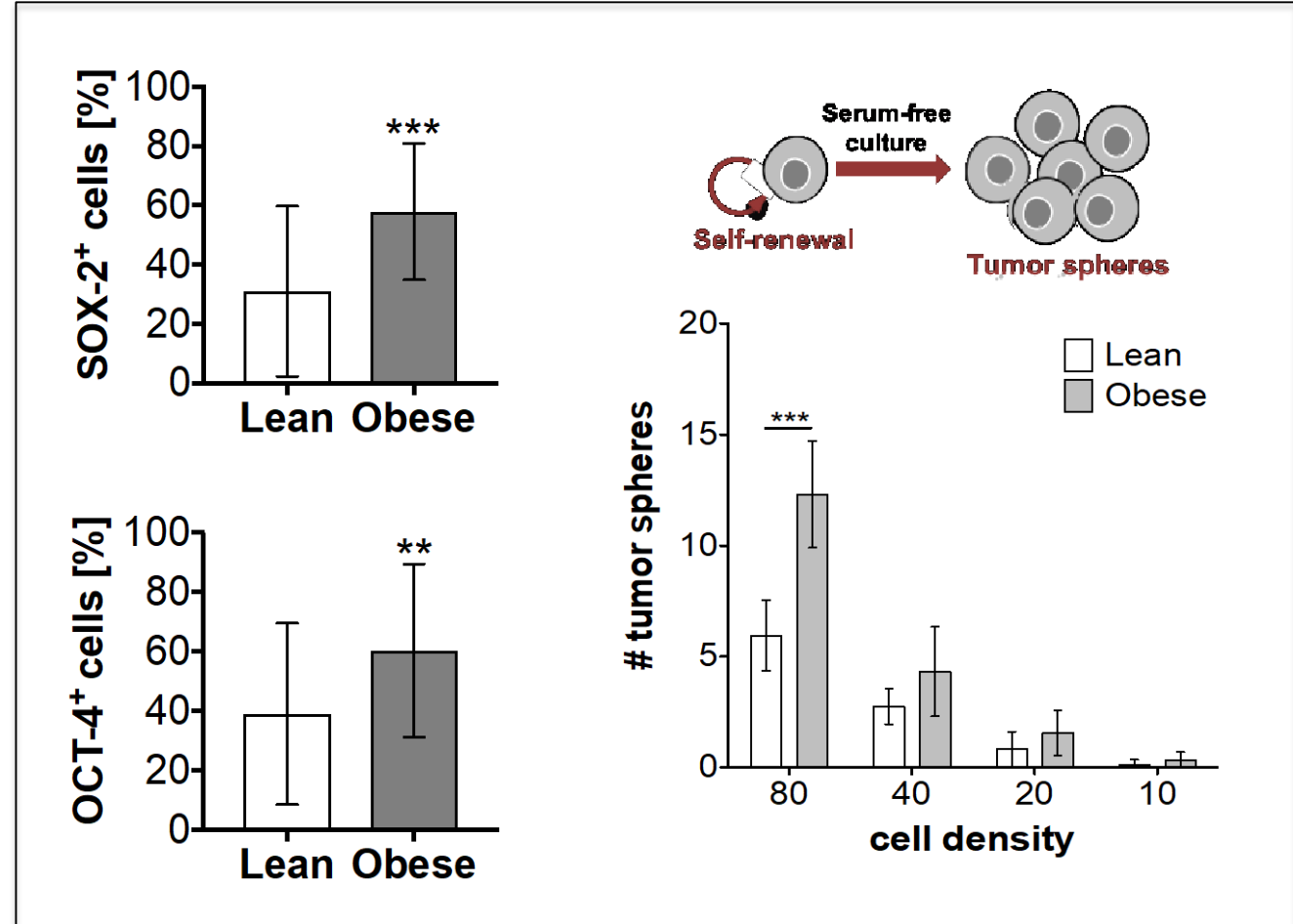
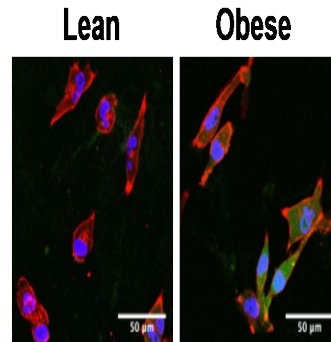
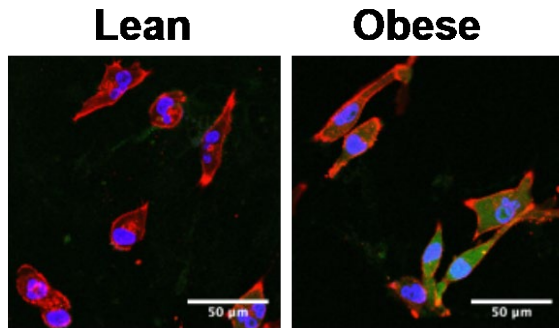
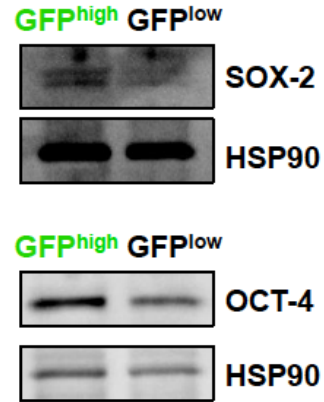
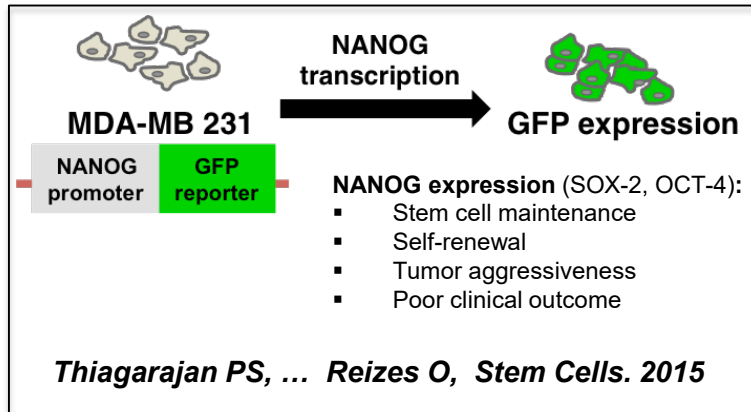


Seo et al. *Sci Transl Med.* 2015

Zheng et al. *Endocr Relat Cancer.* 2013



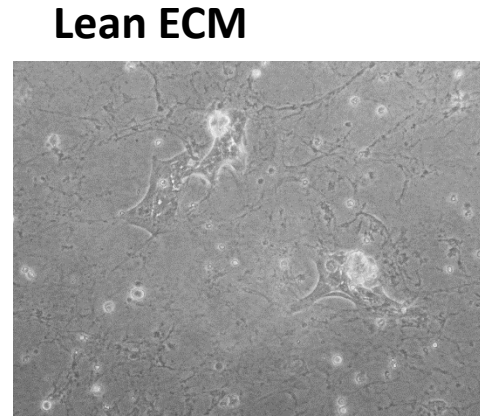
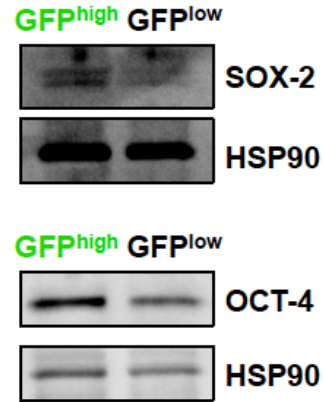
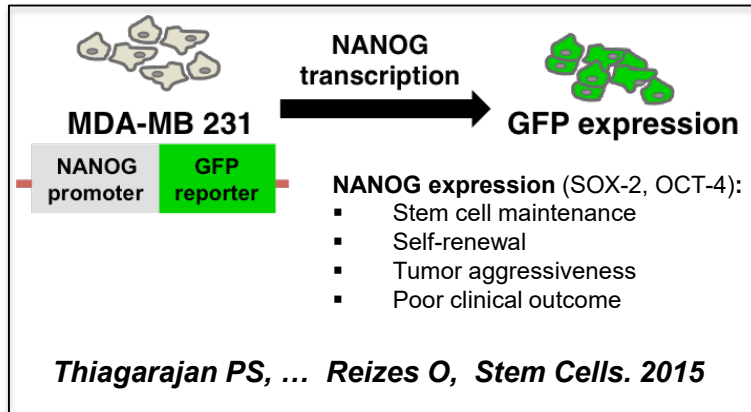
Obesity-associated ECM increases cancer stem cell characteristics in cell lines and PDX spheroids



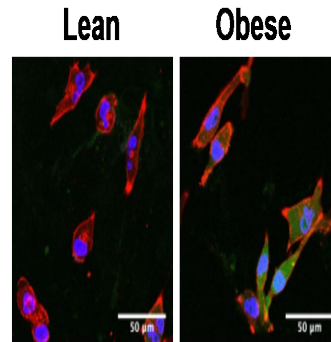
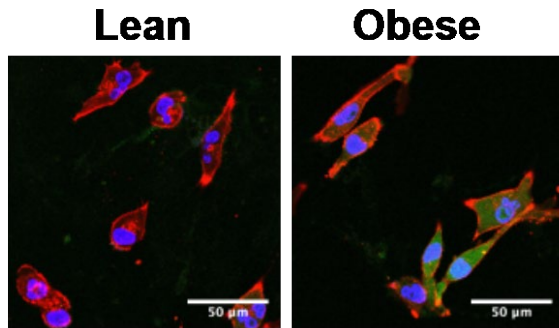
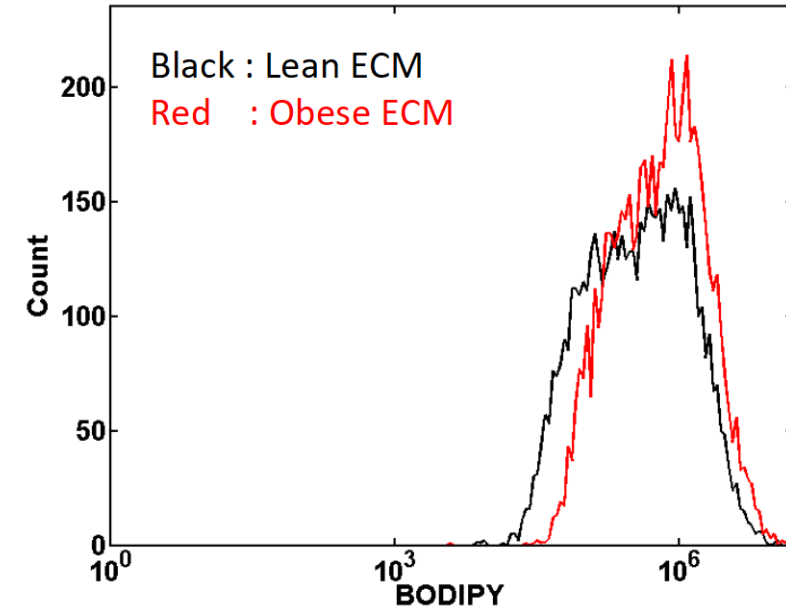
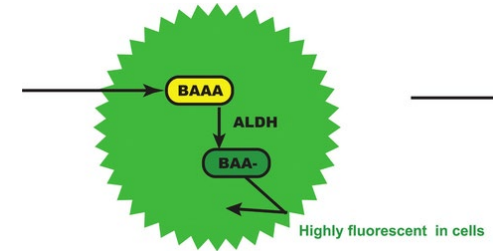
Wittmann K et al., under revision



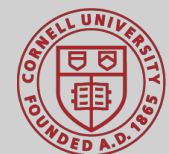
Obesity-associated ECM increases cancer stem cell characteristics in cell lines and PDX spheroids



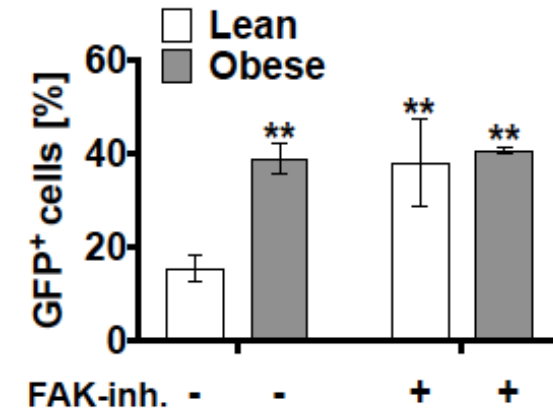
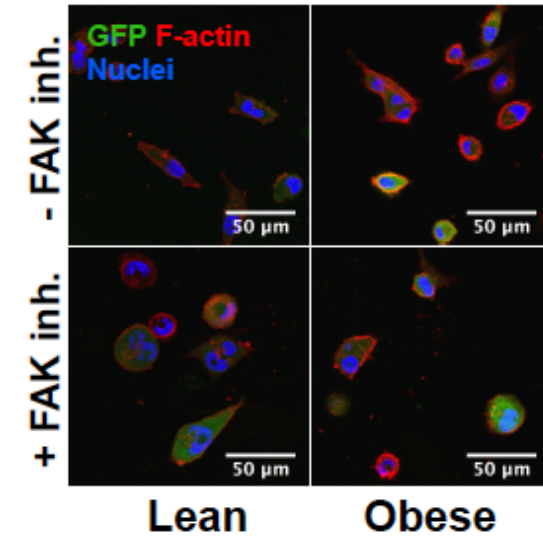
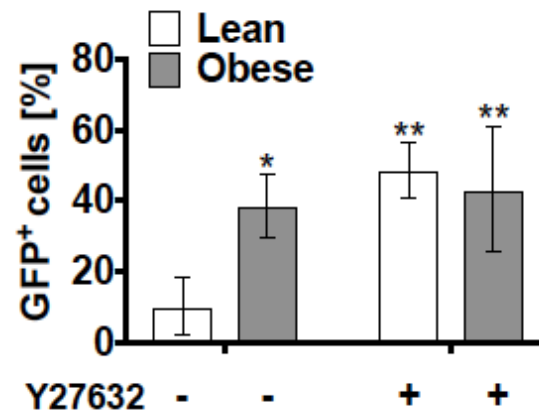
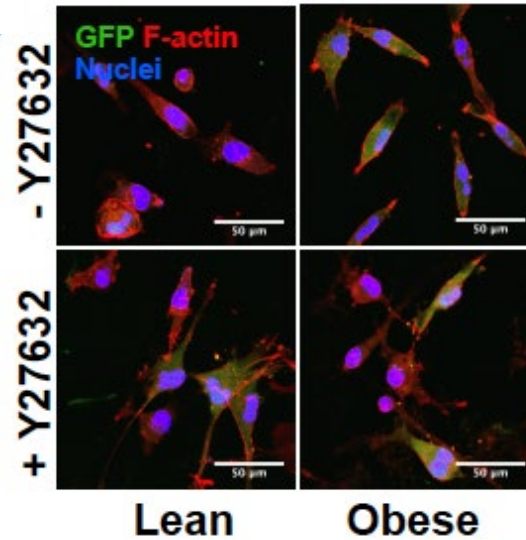
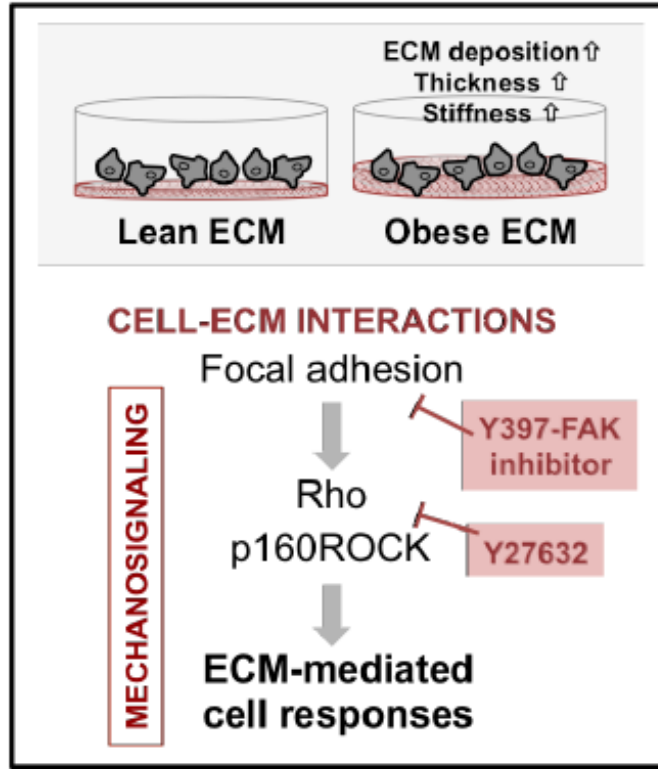
ALDEFLUOR assay



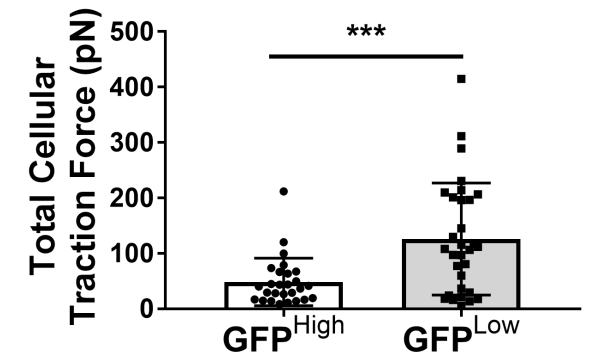
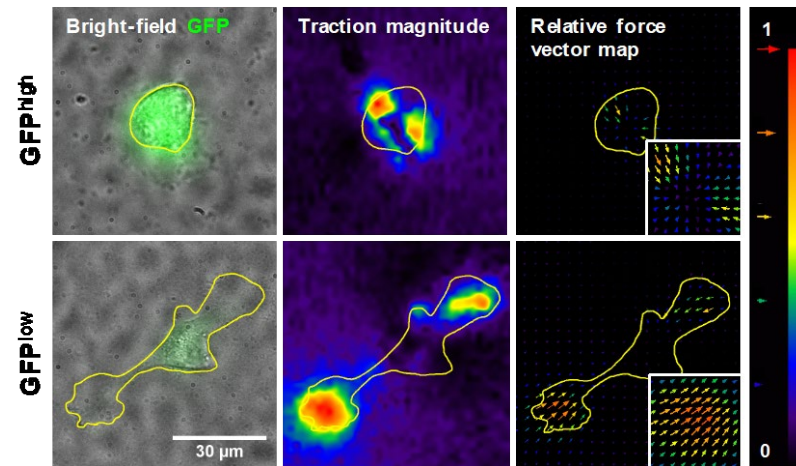
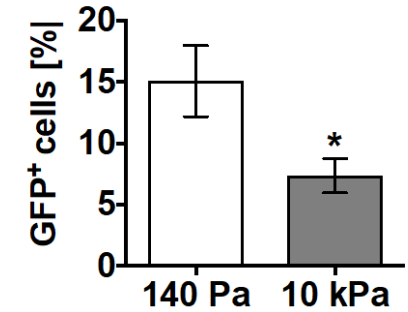
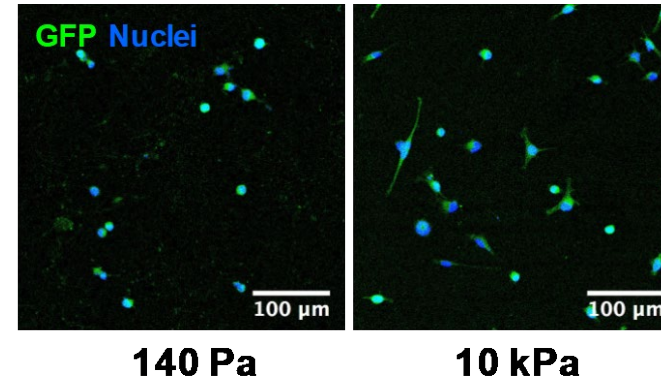
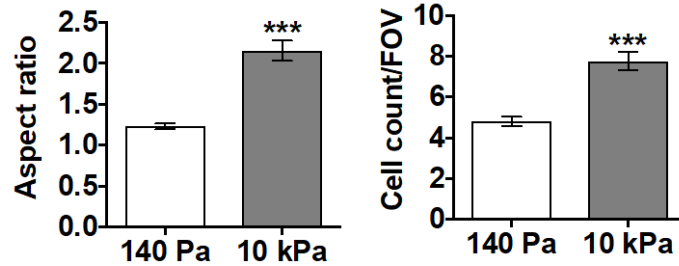
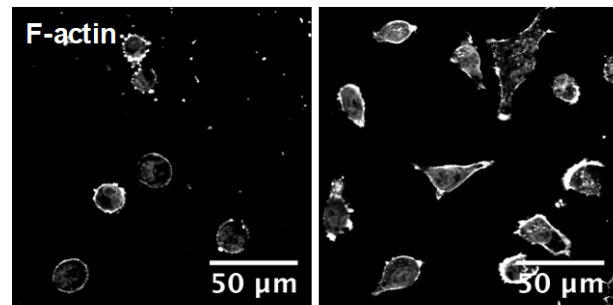
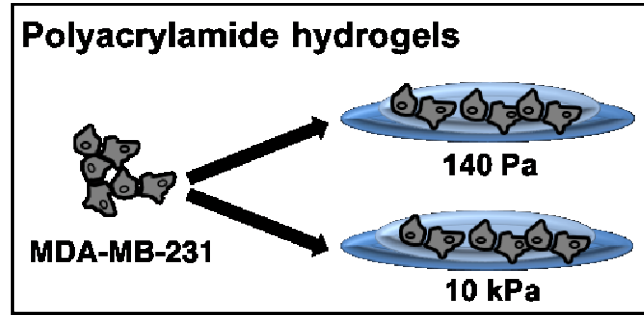
Wittmann K et al., under revision



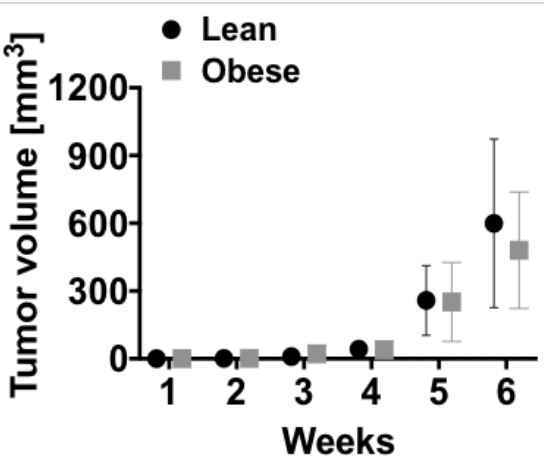
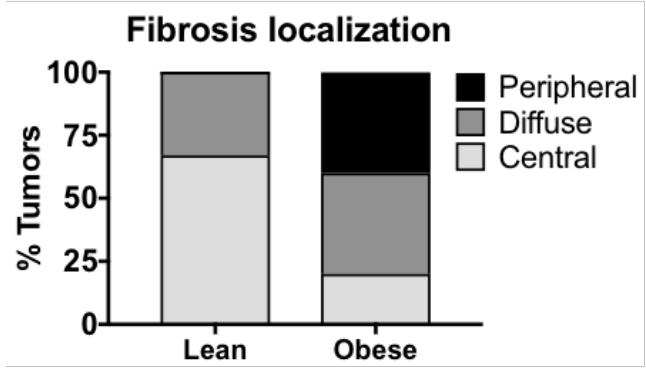
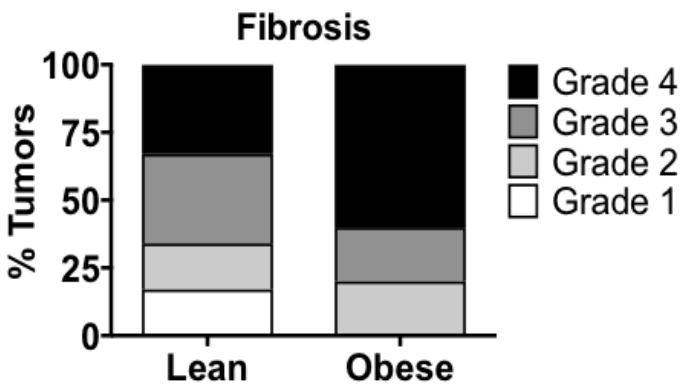
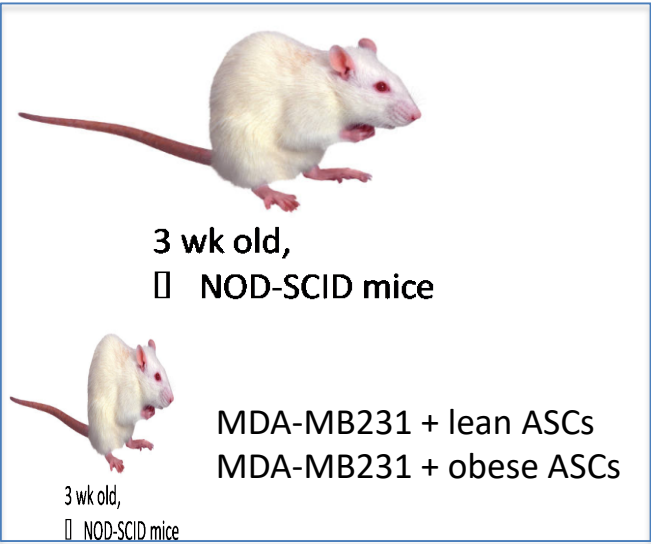
Obese ECM modulates cancer stem cell characteristics by interfering with stiffness sensitivity



Increased stiffness of polyacrylamide substrates decreases cancer stem cell (CSCs) characteristics



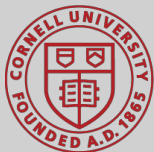
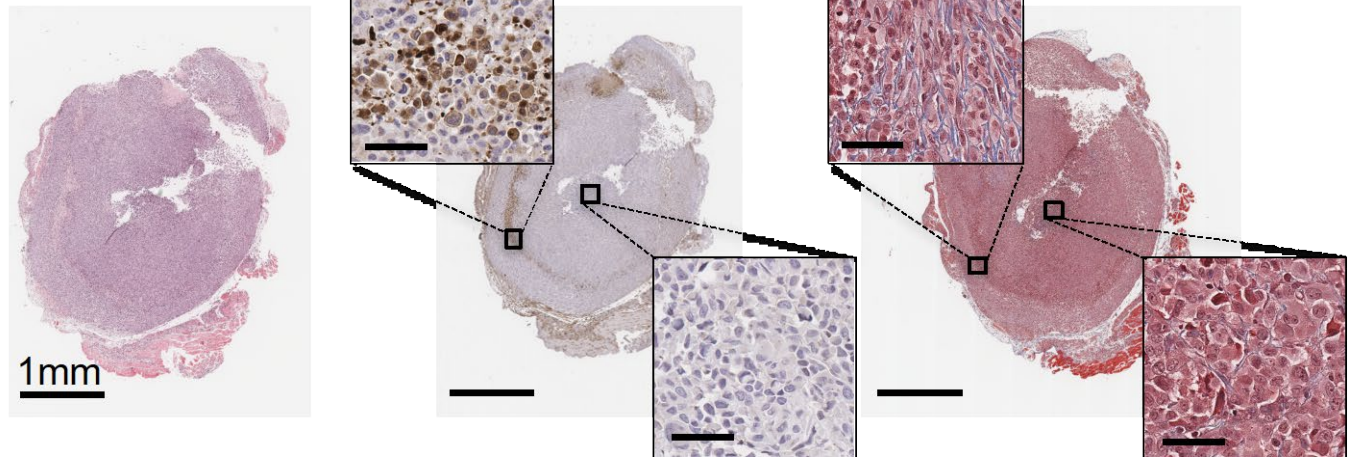
MDA-MB231 xenografts co-implanted with obese vs. lean ASCs have more peripheral fibrosis that coincides with NANOG immunoreactivity



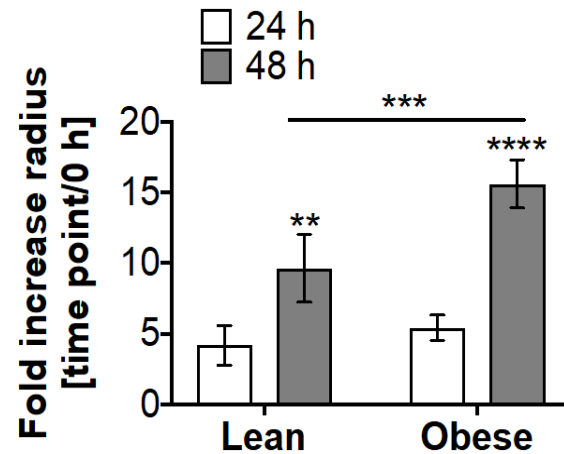
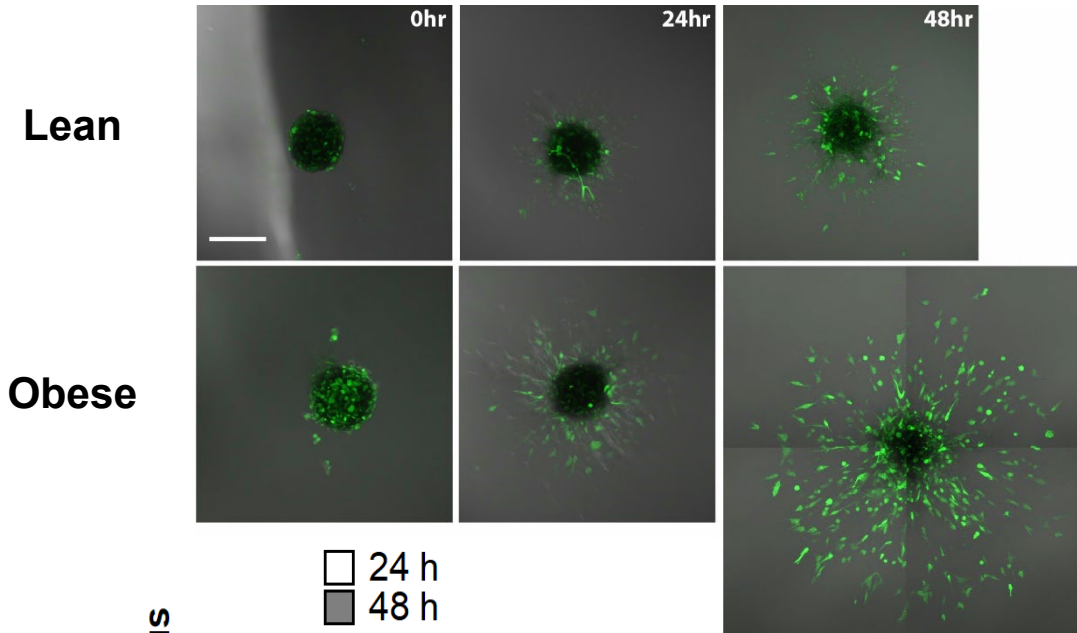
H&E

Nanog IHC

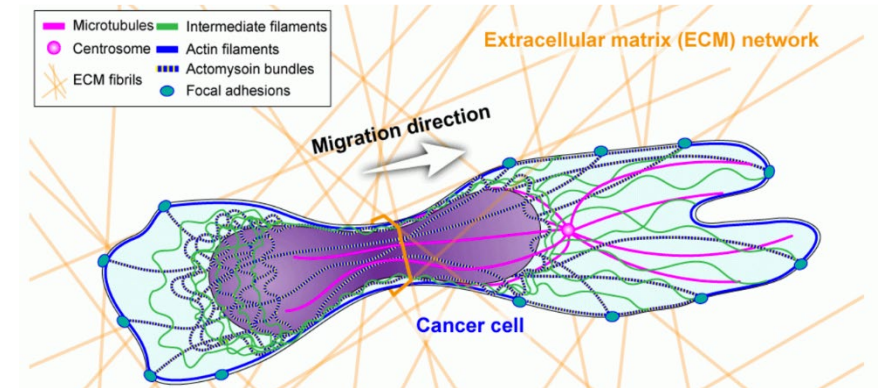
Trichrome



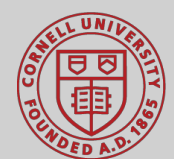
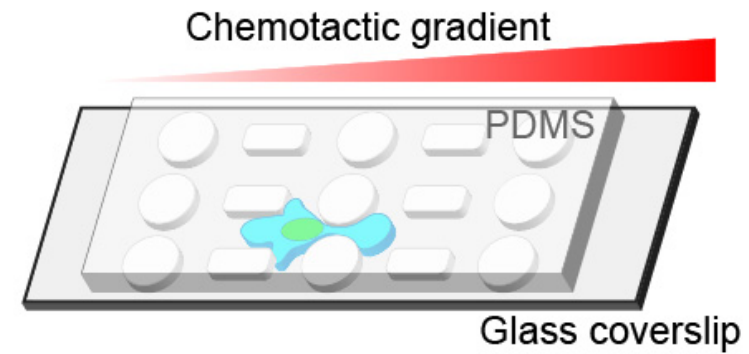
Obesity-associated ECM remodeling promotes invasion



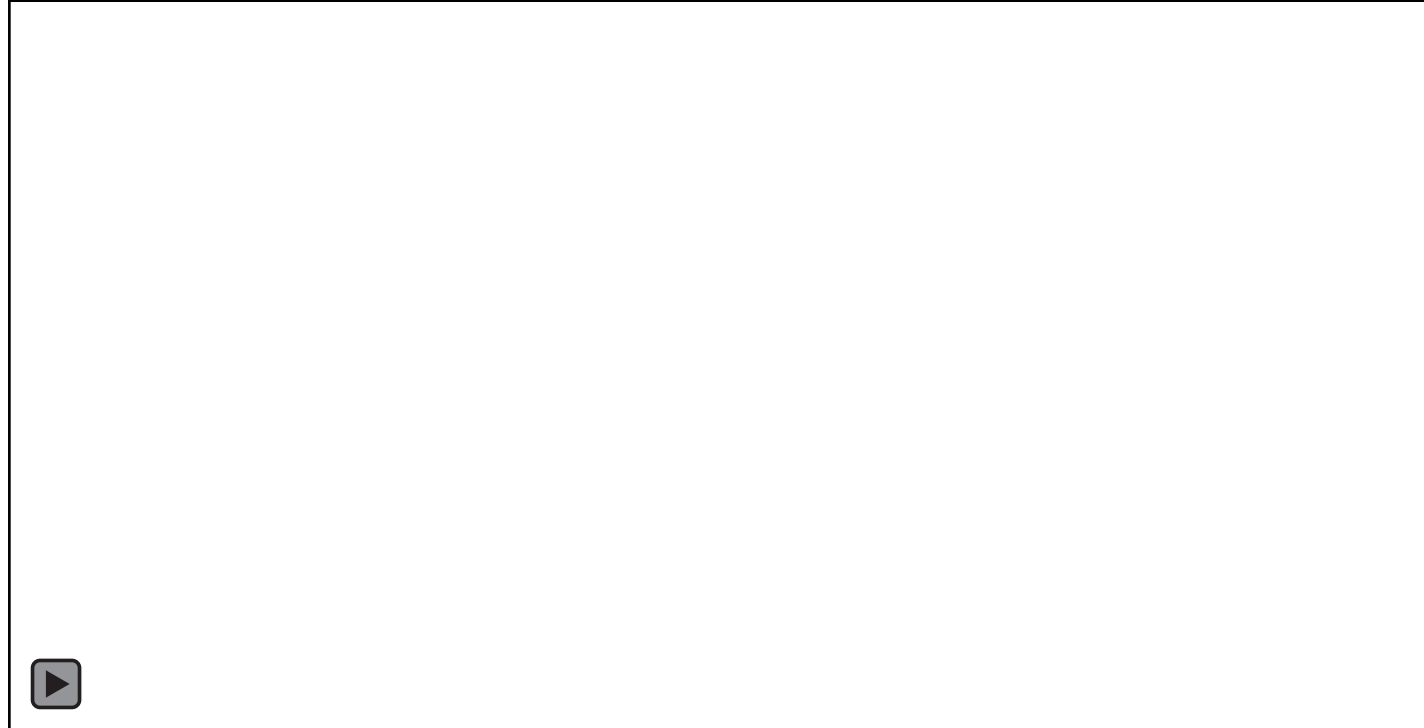
Tumor invasion/metastasis



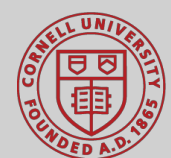
McGregor, Hsia, Lammerding. *Curr Opin Cell Biol.* 2016



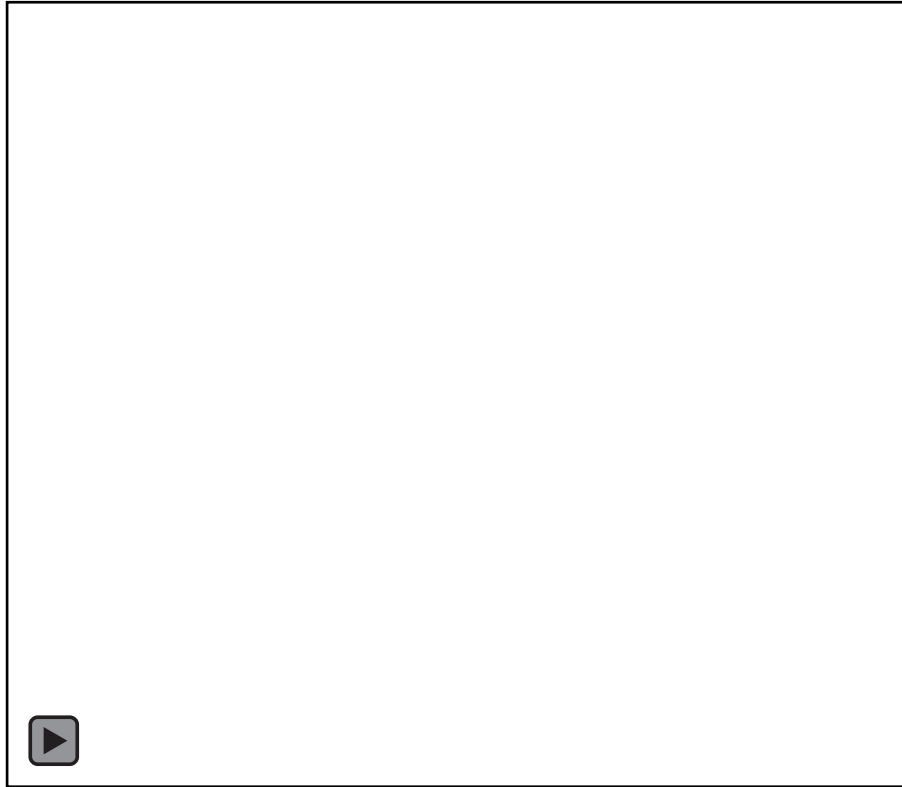
A microfluidic device for precise control of confined migration (Lammerding lab)



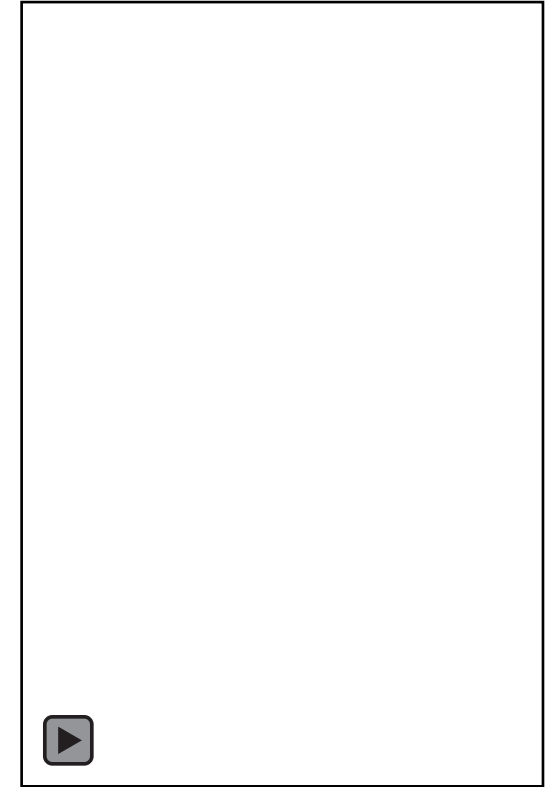
Mouse embryonic fibroblast expressing **mCherry-Histone H4** and **GFP-actin** migrating through a $3 \times 5 \mu\text{m}^2$ constriction



Physical stress can result in transient nuclear envelope rupture and exposes genomic DNA to the cytoplasm

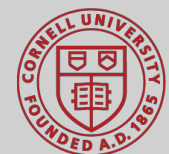


MDA-MB-231 breast cancer cells expressing **NLS-GFP** and **histone H2B-RFP**.

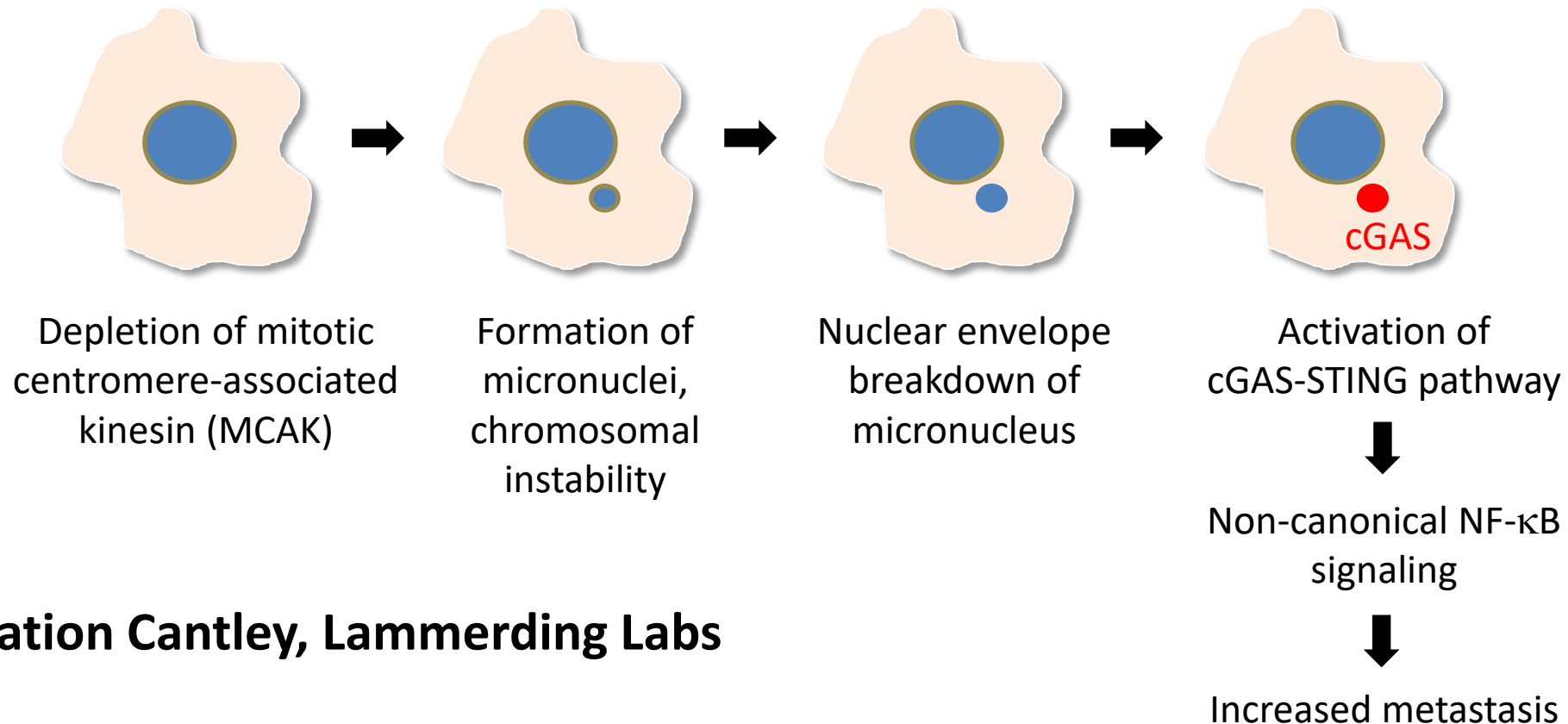


HT1080 fibrosarcoma cell expressing **NLS-GFP** and **cGAS-RFP**.

Denais, Gilbert, Isermann et al. *Science* (2016)



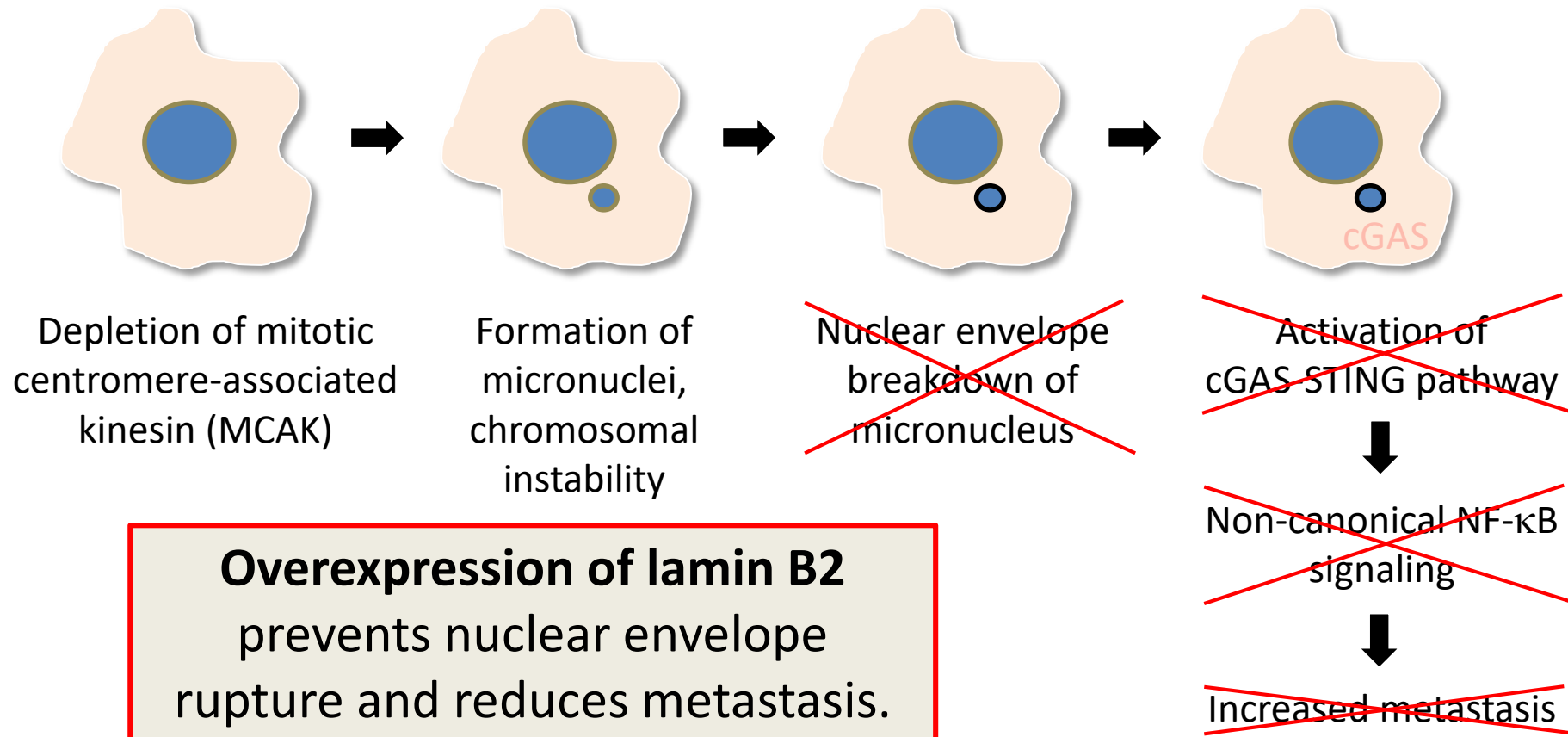
Exposure of genomic DNA to cytoplasm activates cGAS-STING pathway and promotes metastasis



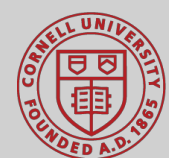
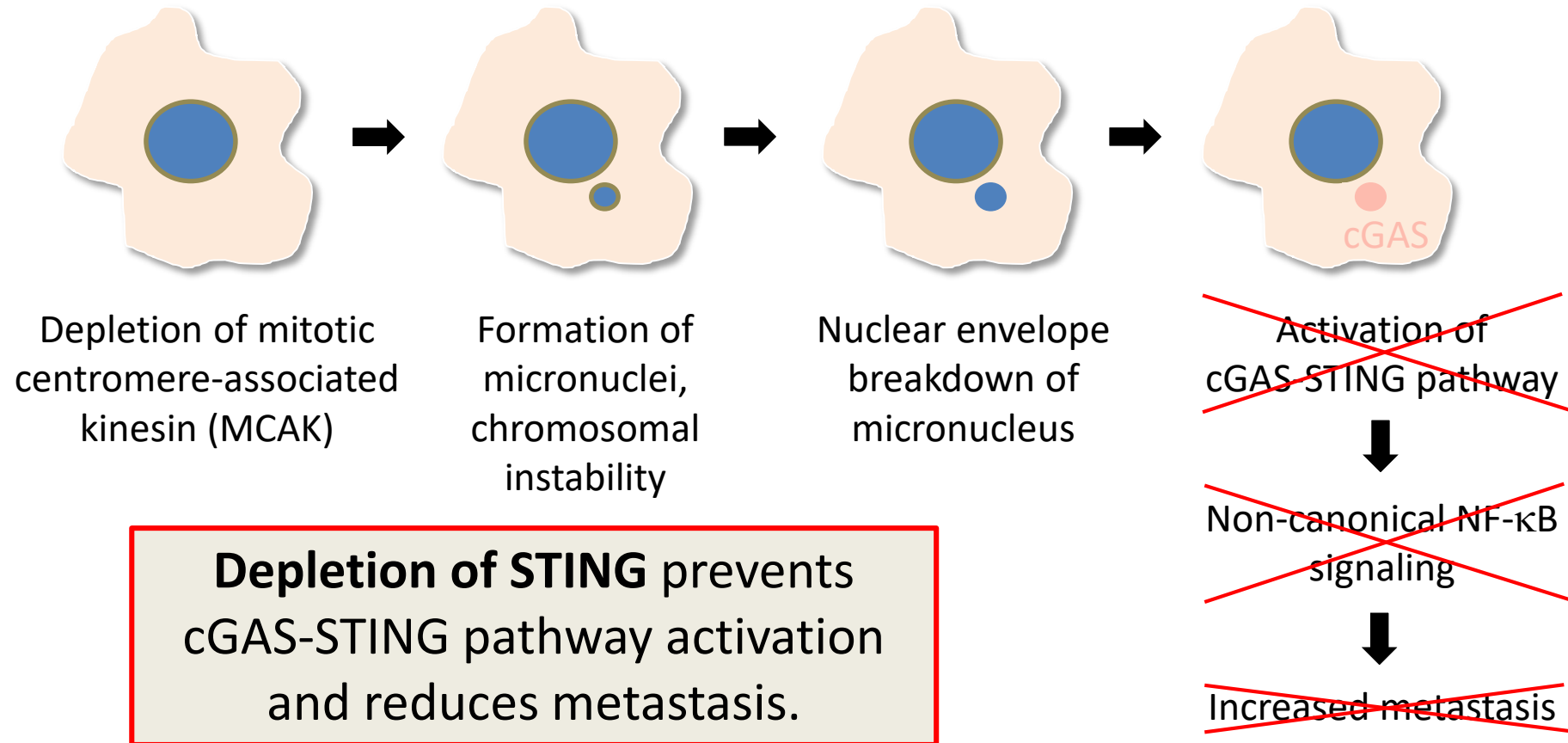
Collaboration Cantley, Lammerding Labs



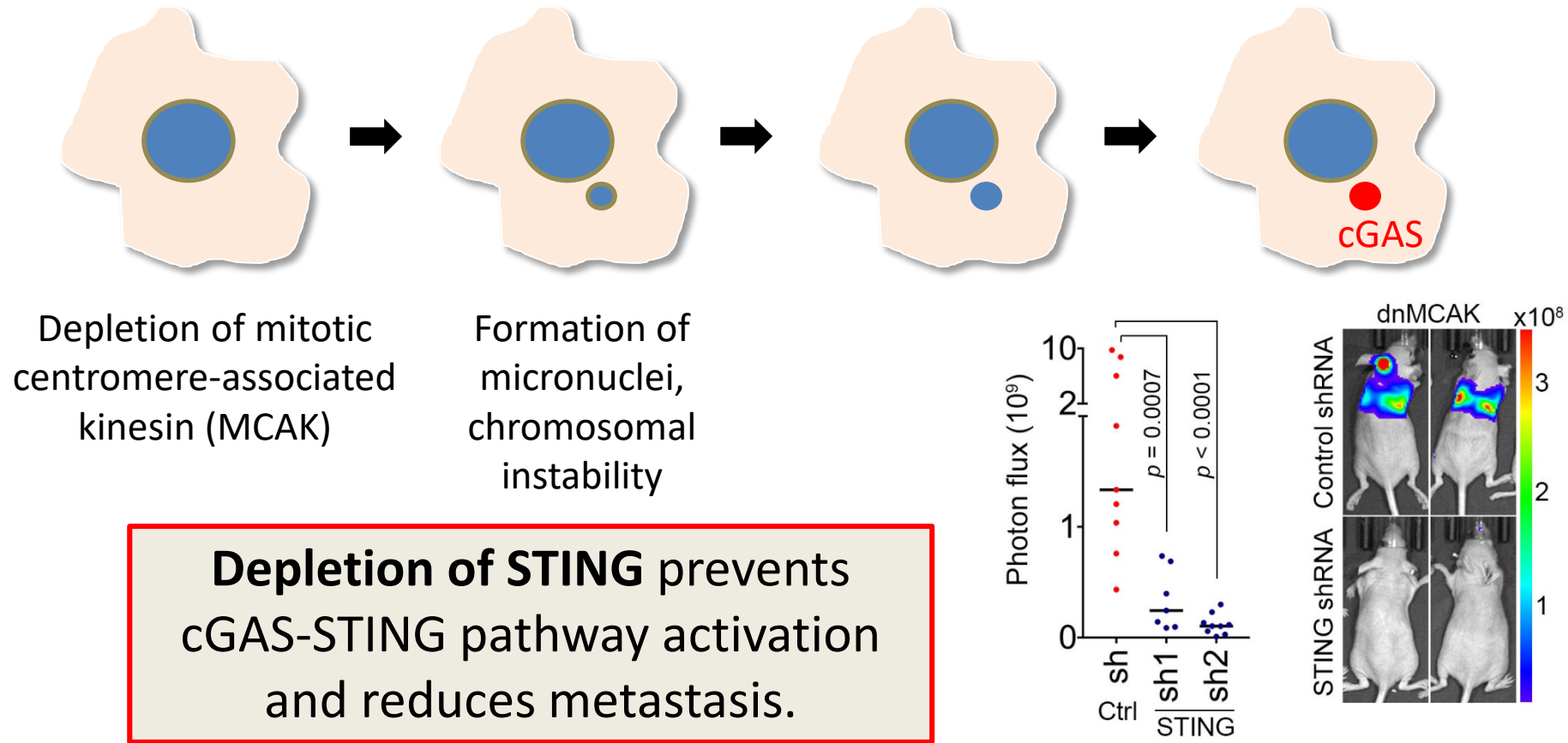
Exposure of genomic DNA to cytoplasm activates cGAS-STING pathway and promotes metastasis



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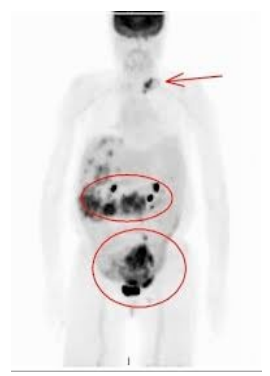
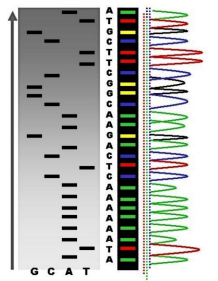


Exposure of genomic DNA to cytoplasm activates cGAS-STING pathway and promotes metastasis

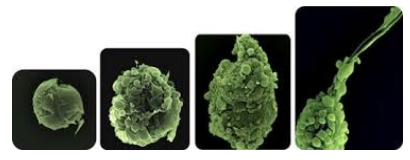


Current and Future Directions: Developing Experimental Therapeutics

Englander Institute for Precision Medicine, Sequencing



Biobanking



Organoids

Drug screening



Analysis in microdevices

Mouse models



Clinical trials

Image-guided tumor biopsy

