Companion PowerPoint slide set Obesity-associated breast cancer risk: a role for epigenetics?

Dr. Liza Makowski

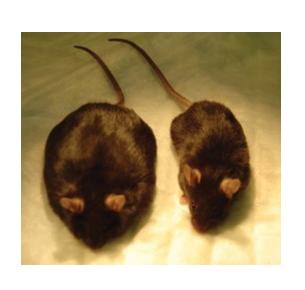
Studies Basal-like Breast Cancer (BBC)

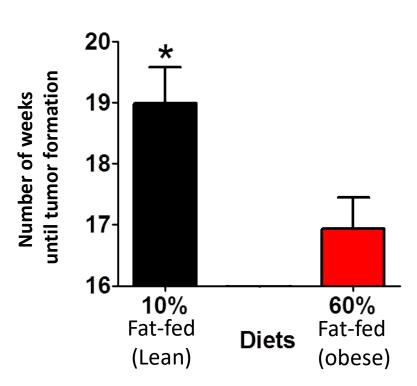


- Aggressive cancer
- No specific drug therapies
- Short survival time if it spreads beyond breast tissue (metastasis)
- More prevalent in young pre-menopausal women
- More prevalent in African Americans
- Obesity is a risk factor for all breast cancers

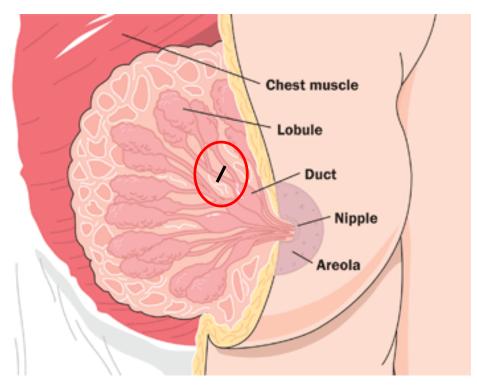


Obesity causes BBC tumors to form at a faster rate compared to lean mice



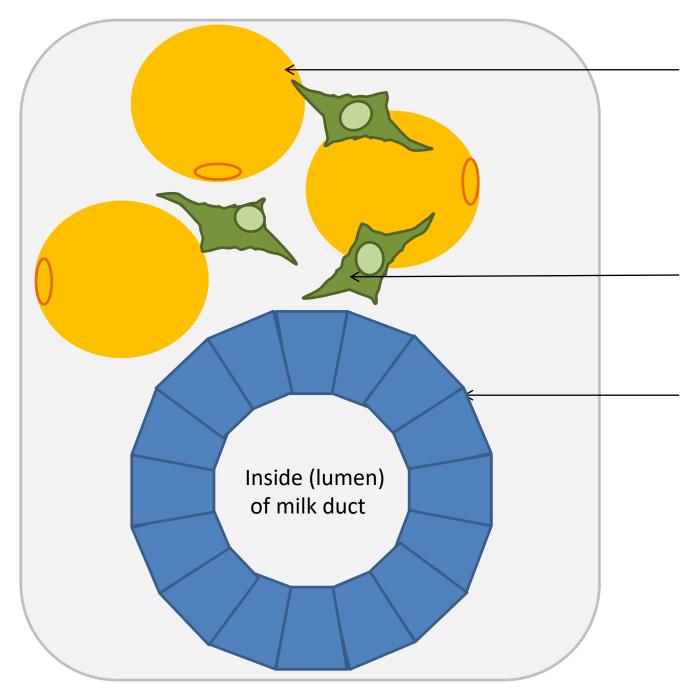


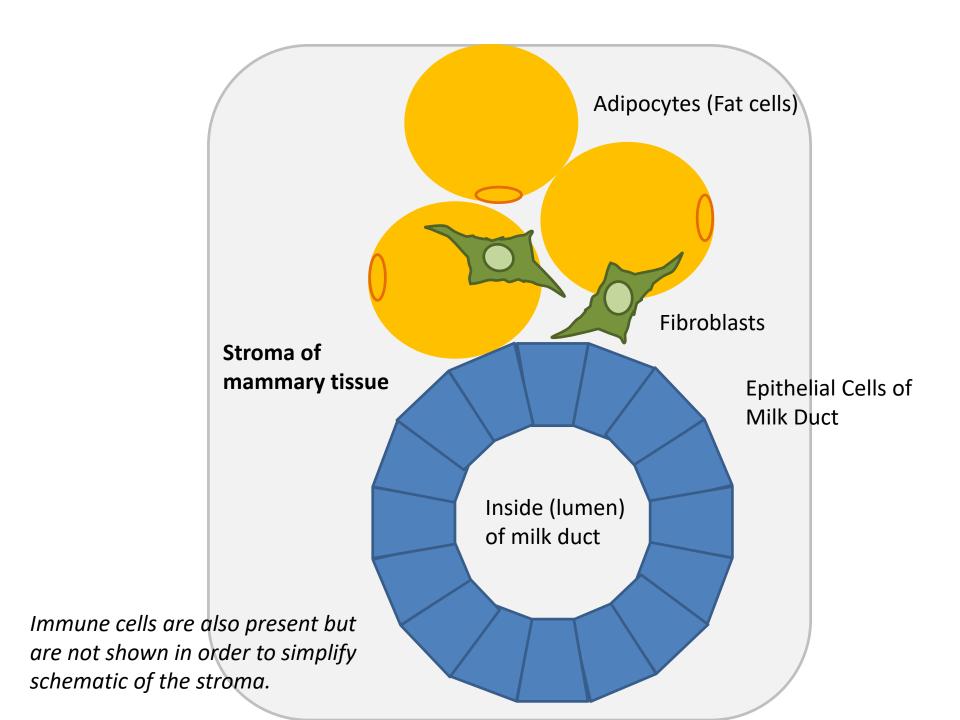
Cross-section of mammary (milk) duct



http://www.womenshealth.gov/breast-cancer/what-is-breast-cancer/

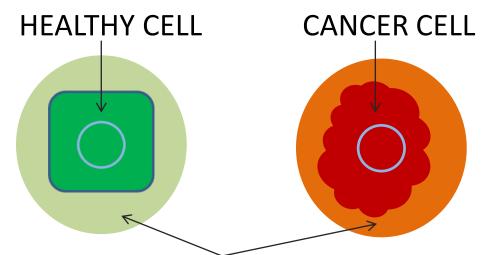
Label **epithelial cells, fat cells and fibroblasts** on the diagram below:







Cancer & the microenvironment

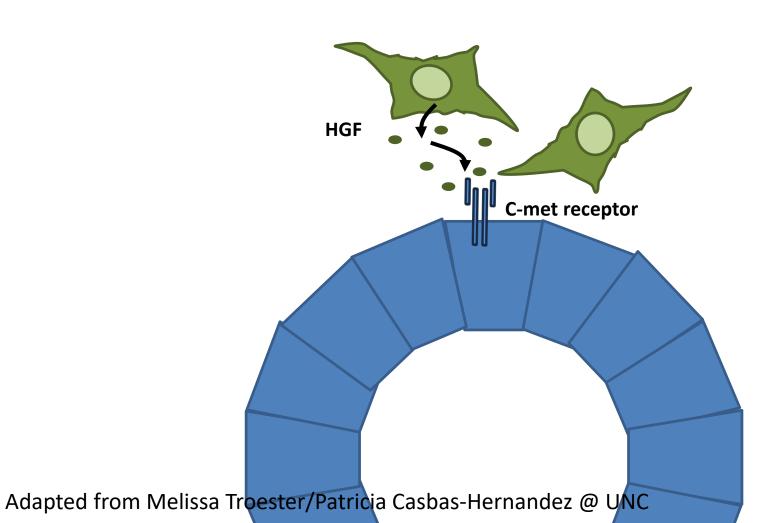


The microenvironment ("soil") surrounding a cell ("seed") plays a role in tumor formation.

Liza Makowski: "How does obesity alter the microenvironment in breast cancer?"

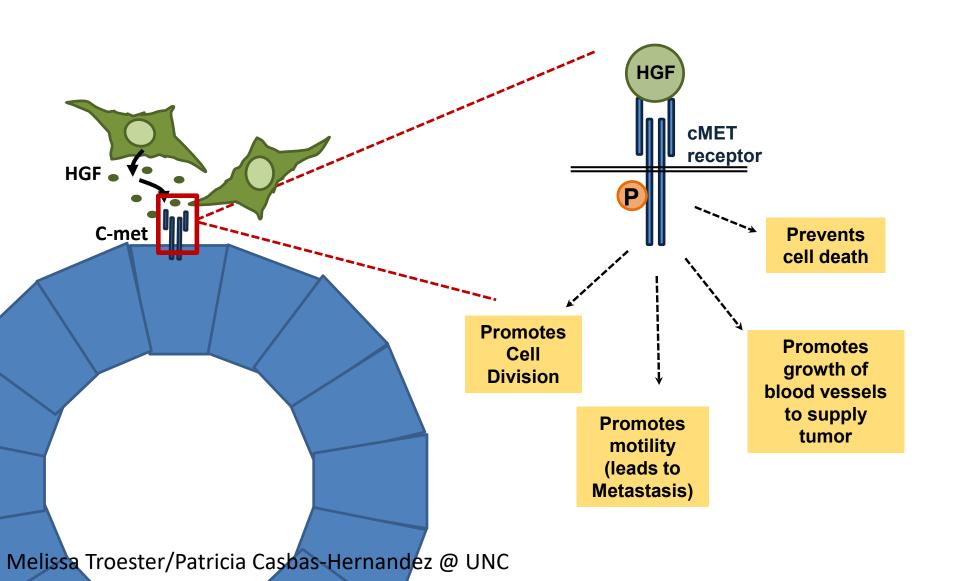


Cell to cell communication HGF-cMET paracrine signaling



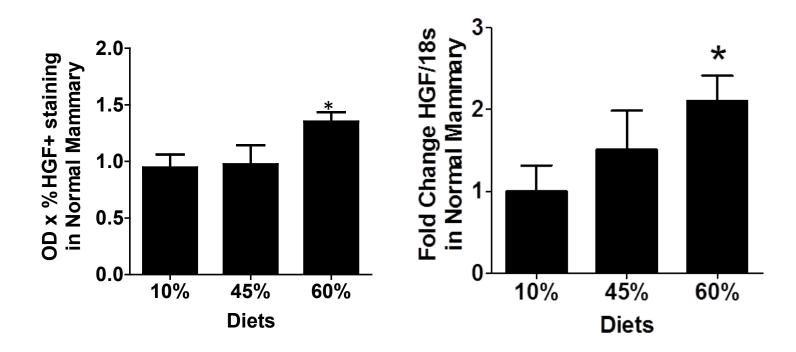


Cell to cell communication HGF-cMET paracrine signaling





Obesity increases levels of HGF mRNA and protein in normal mammary tissue

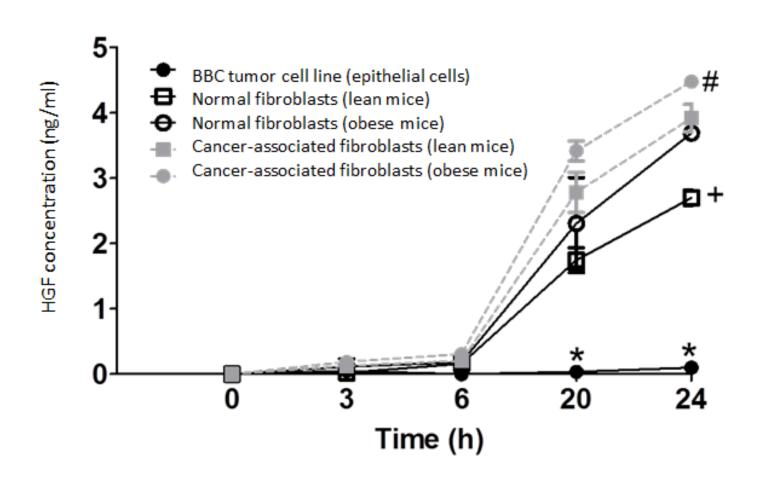




Ex vivo cell culture model

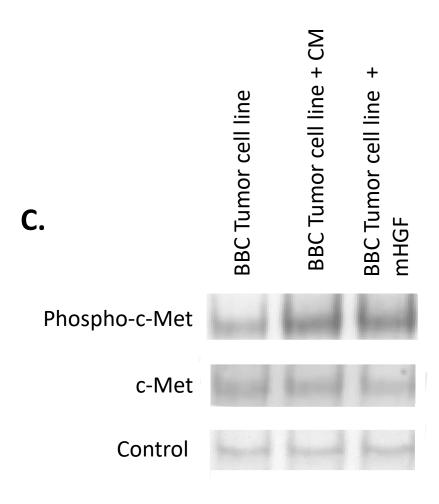
Lean Mice	Isolate Fibroblasts		Culture Fibroblasts		Measure
	Norma			→	HGF Secretion
	Cancerassocia				HGF Secretion
Obese Mice					
		/ →		→	HGF Secretion
		, ————————————————————————————————————		→	HGF Secretion

HGF secretion in cultured cells



Lean Mice	Isolate Fibroblasts		Culture Fibroblasts		HGF Secretion	
	Normal	/ →		→	•••	
Obese Mice	Cancer- associated			→		
		<i>,</i> ——>			•••	
				→		

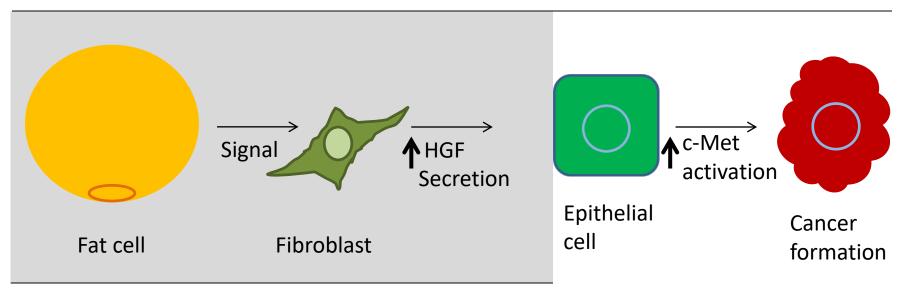
Analysis of c-Met protein levels in BBC tumor cell line







"How does obesity alter the microenvironment in breast cancer?"



Microenvironment

Conclusion: growth factor signaling pathway (HGF/cMet) was upregulated with obesity.

