Center for Environmental Health and Susceptibility

Obesity-associated breast cancer risk: *Modeling the Microenvironment*

This hands-on activity enables students to construct models of a lean and obese breast microenvironment and can serve as an *EXTENSION* to the lesson titled *Obesity-associated breast cancer risk: a role for epigenetics? An examination of evidence.* This activity was developed by Liza Makowski, Ph.D. and her research team in collaboration with the UNC Center for Environmental Health and Susceptibility.

Learning Objectives

By constructing a model of the microenvironments of lean and obese breast tissue students will be able to:

- Compare the microenvironment of lean versus obese breast tissue and discuss implications for diseases like breast cancer;
- Model the interactions between the following cell types and structures in mammary tissue: adipocyte (fat) tissue, blood vessels, immune cells (macrophages and T cells) and the c-Met receptor and its ligand (HGF).

Preparation

Use the table below to assemble the materials to be used to construct models. A candy and non-candy option is provided. For either option, students asked to construct obese models will not only use larger "fat" cells but will also use *more* of the materials for their model (e.g., more blood vessels, more c-Met receptors, etc.). Paper plates or pieces of paper will represent the epithelial surface of the mammary duct (the surface facing the stroma).

Cell type	Candy equivalent		Non-candy equivalent	
	Lean	*Obese*	*Lean*	*Obese*
Adipocyte (fat) cell	Mini Marshmallows	Large Marshmallows	Small cotton balls	Large cotton balls
Blood vessel	Licorice wheels (unwind and cut)		Red pipe cleaner	
Macrophage	Mini Reese's Peanut Butter Cup DARK *(anti-inflammatory)*	Mini Reese's Peanut Butter Cup ORIGINAL *(pro-inflammatory)*	Small green pom-poms *(anti-inflammatory)*	Small pink pom-poms *(pro-inflammatory)*
c-Met receptor (*on epithelial cells*)	Life Savers gummies		Paper clips	
HGF (ligand) *Fibroblasts not included in model*	Gummy bears or small round gummy candies		Hole-punch remnants or confetti	
T (immune) cells	Skittles		Colored beads	
Epithelial cells	Paper plate surface			

Activity Procedure

1. Tell students they are going to use materials to construct models of the breast microenvironment in an effort to visualize interactions between the following cell types and structures in mammary tissue: adipocyte (fat) tissue, blood vessels, immune cells (macrophages and T cells) and the c-Met receptor on epithelial cells and its ligand (HGF) which is produced by fibroblasts.
2. By constructing these models and comparing lean versus obese microenvironment, students should consider how the microenvironment (stroma) of the breast tissue might contribute to breast cancer onset.
3. Provide students with the materials to construct either a lean or obese microenvironment.
4. Ask students to record their observations on sheet of paper or notecard and place by their model.
5. Next, ask students to observe either a lean or obese model from another group for comparison.
6. As a class, discuss the differences observed between the two microenvironments and discuss the implications for disease, specifically BBC.
7. Remind students that researchers know that *interactions* between the cells of the stroma and epithelial cells in mammary tissue are important in the formation of breast cancer and that **obesity has been observed to affect the mammary stroma.** H**epatocyte growth factor (HGF)** is made and secreted by fibroblasts and imparts a response in neighboring (local) epithelial cells via a **receptor protein** called c-Met (mesenchymal-epithelial transition factor (MET) receptor). c-Met activation leads to cell proliferation (tumor cell growth), angiogenesis (growth of blood vessels necessary for tumor to get bigger), and metastasis (ability of cells to move and spread across body). Many drug companies are looking at c-Met inhibitors for breast and other cancers.