Teachable Unit: Executive Summary

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Title: The Role of the Cytoskeleton in Cell Adhesion and Migration

Team III: Cell/Molecular Biology

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I. Learning Objectives

Students would be able to: assemble a diagram of the actin cytoskeleton structure and interaction with the cell membrane; predict the effects of drugs that target cellular components and effects on modulating cell adhesion and cell motility in normal and diseased (cancer) states.

A. Science Content: Students will learn that:

1. the cytoskeletal network links the inside of a cell with its external environment
2. attachment of a cell to the extracellular matrix (ECM) depends on dynamic interaction through actin filaments and their accessory proteins
3. detachment of a cell from the ECM requires changes in protein-protein interactions that link the intracellular environment with the extracellular environment.
4. metastasis occurs when tumor cells alter their actin filament network, disrupting their attachments to the proteins in the extracellular environment.
5. drugs can target cytoskeleton formation to be used in therapeutic applications.

B. Science Skills: By the end of the teaching unit, students should be able to do the following:

1. identify the various components of the cytoskeleton and describe their function
2. recognize the dynamic nature of the cytoskeleton in cell motility and adhesion
3. predict the effects of a drug on the cytoskeleton in cell motility and adhesion
4. communicate the relationship between cell movement and cancer metastasis

C. General Skills: Students would have assembled a general framework for acquiring knowledge through investigation.

II. Teaching Challenge

A. Science Content:

Students enter the classroom with a number of misconceptions about cell architecture, how cells move, and how they attach. These initial misunderstandings are inconsistent with how cell structure influences cell movement.

1. Students think that all cells are round.
2. Students think that cells float, they don't move.
3. Students think that blood moves cells.
4. Students think that actin is found only in muscles.
5. Students think that the cytoskeleton is not dynamic: it does not move.

III. Brief description of the teachable unit

A. Context

The teaching unit is based on previously assigned out-of-class activities: reading assignment, homework and online quiz. Students have already learned about actin filament polymerization and de-

polymerization, and the intracellular dynamics of the cytoskeleton. This teaching unit bridges what happens on the inside of the cell to the outside environment of the cell.

This teaching unit begins with a brain storming activity that lists possible answers to questions on cell motility and adhesion. During the teaching unit, an analogy for cell attachment is used by relating a cell to a boat with anchors at the front and back. Students use the boat model as a simple introduction to their understanding of cell adhesion and cell motility, and become familiar with directional cell movement associated with a cell's *leading edge and its trailing edge*. The students then use this simplified molecular model to relate key components of intracellular protein structures to protein-protein attachments that form in the extracellular environment. This work leads to a series of in-class clicker questions, allowing the instructor to gauge students' knowledge, understanding, and application of the model.

Students subsequently are given examples of drugs that disrupt actin filament structure to enhance their understanding of this topic. This in-class activity ends with a homework assignment that will be posted online, which students will bring to the next class.

B. Overall Sequence of Activities

The in-class portion of this teaching unit begins with a brain-storming activity on, "Why do cells move?" and, "Are there situations when cells move when they should not?"

1. Students are shown a picture of a boat with 2 anchors (one anchor at the front and one anchor at the back of the boat) representing a cell anchored (attached) at opposite ends of the cell. Students use this simple analogy to relate to cell attachment and to cell movement. Students predict how removing an anchor allows a cell to move in a directional pattern.
2. Students then use a simplified molecular model showing key cellular protein components that demonstrate how cofilin cuts actin filaments inside the cell, and releases the tension on the transmembrane integrin proteins, which allows the cell to detach from its extracellular connections. (Please refer to model shown in Figure 1 at the end of this report.)
3. The students use two models for cell movement and adhesion to solve a real cell problem:
    a. On the left side of the molecular model, the actin filament is not cut because cofilin is inactive, and the cell remains attached due to the transmembrane integrin proteins linking the cell to its outside environment.
    b. On the right side of the molecular model, the actin filament is cut by cofilin, causing the integrins to change conformation, and releasing their attachment from the ECM.
    c. In our model, the integrins are the anchor, the cofilin cuts the actin filaments, which are the ropes that hold the anchor.
4. Ask an interactive clicker question:
    a. "Which side of the cell would you expect cofilin to be more active: the leading edge or the trailing edge?"
    b. We poll the class, and ask students to explain their answers: A (trailing edge) and answer B (leading edge). We then tell students the right answer after they explain all of the options in their answers.
5. Ask an interactive clicker question:
    a. What happens if cofilin cuts actin filaments at the "leading edge" of the cell? Poll the students first, using clickers.

b. Ask them to talk to their neighbor, and re-poll the students. Ask a student to answer who has changed their answer and explain why. Tell them the correct answer is : "Cell stops migration"

6. Ask another clicker question, "Which of the following mimics cofilin activity?" Ask the students to figure it out as a team. Poll the students. Ask them for the incorrect answer first. Then explain the correct answers. Tell them the correct answers.
7. Post the final assignment on Blackboard. An assignment can ask students to predict how a drug that alters actin filament structure will influence how a cell functions. Then ask a question that proposes using a drug that interferes with integrin binding to the ECM, and is used in treating breast cancer. Ask students to use the model for cell movement and adhesion to explain how the drug affects breast cancer. The assignment can help assess how well students understand and apply their knowledge of actin filament structure and function.

IV. How does the Teachable Unit address the following themes?

A. Diversity

Cell movement and adhesion is of broad interest to biology and other science majors, because of its important role in normal cell development, wound healing and tissue regeneration, immune responses, and in cancer metastases.

A series of questions have been developed to measure students' knowledge, understanding, and application, as well as brainstorming activities to probe and draw out student knowledge gaps and prior misconceptions about the subject matter. These include questions that probe students' knowledge and conception of cell shape and architecture, cell size, internal cellular architecture, and the dynamic nature and properties of the cytoskeleton

Those students with different backgrounds (non-Biology majors) may have different sets of knowledge gaps and misconceptions, but they also offer an opportunity to promote unique perspectives to problem solving. For example, students can identify diseases that affect aspects of the cytoskeleton, create a team-based problem-solving activity, and utilize the unique backgrounds of the team members to solve their problem.

B. Active Learning

Students' interest will be caught by the relevance to the development of metastatic cancer as well as normal development. Most students are familiar with cancer and cancer spreading (metastasis), a disease that may have affected a family member or friend. For our specific teachable unit, we have developed a set of activities that engage students in working with a model-based inquiry learning activity. This activity probes their ability to explore a model and make predictions from this model about the cytoskeleton, cell adhesion, the extracellular space, and how these structures interact in the dynamic process of cell migration.

C. Assessment

These include: pre-reading, pre-class quiz, in-class formative assessments (i.e., Clicker questions), after-class follow-up homework, writing a short answer response to a question or topic on the subject, as well as summative assessments that relate to the topic.

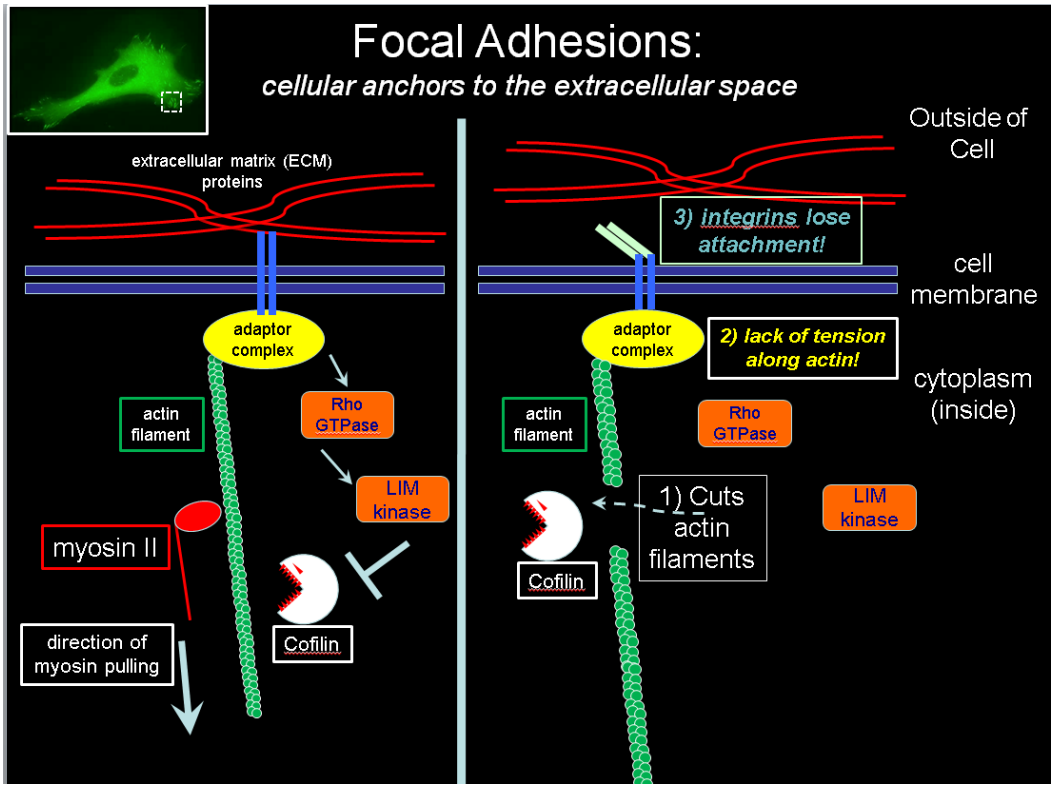

Figure 1. Simplified molecular model illustrating cell attachment and detachment through actin filaments.