Supplemental Material

CBE—Life Sciences Education

Bierema *et al.*

Supplement 1. Instruction materials.

Biotechnology Course: Self-Renewal

Model Resources

- Read Chapter 9 sections 1, 3, 4, 5, and 6 in the e-text.
- Read parts I and II of "Stem Cell Basics". http://stemcells.nih.gov/info/basics/Pages/Default.aspx
- Complete the Mastering Biology Homework on Mitosis, Stem Cells, and Regenerative Medicine.
- Complete the outline on Mitosis, Stem Cells, and Regenerative Medicine.
- Watch the recording on mitosis. https://mediaspace.msu.edu/media/Mitosis/1_pvvi5wad

Model Development

Information from the pre-class recording, the homework, and the article stem cell basics discussed how cells divide and the self-renewing property of stem cells. Your goal is to develop a model that explains how one cell produces two cells with identical genetic information. Your model does not need to include every detail of mitosis, just the key details you think are required to explain how two new cells with identical genetic information are produced.

1. Make up a drawing that represents the how one stem cell can self-renew to produce two new stem cells. Focus on the genetic information in the stem cell. Your model must include some depiction of DNA as a polymer made of monomers and why this is important for producing cells with identical genetic information. You should label the key features needed to explain why the genetic information is the same in both cells.
2. Write a brief paragraph explaining how your model shows what happens to the genetic information of stem cells during self-renewal. The paragraph must have a least **two linked cause and effect statements**.

As you develop the model with your team, be sure to discuss which features should be included and **why these features are important for explaining the overall causal relationships** required to explain how stem cells self-renew and proliferate. Remember, the goal of developing this model is to help you make sense of how stem cells self-renew and proliferate. Your model (drawings and explanations) must fit in one document or on one piece of paper. Your group must be prepared to present your model to the class.

Model Presentation and Feedback

As each group presents their model, think about how their model differed from your model. Concentrate on the features you labeled and the relationship between these features and the causal explanation. Think about how you might improve either their model or your model based on the differences. **Your feedback should include specific details to improve the model.** After the group finishes presenting their model, discuss in your group what feedback you might give that group to help them improve their model. Your feedback must include one of the following:

- Something they should add to their model and explain how this would improve their model.

- Something they should remove from their and explain how this would improve their model.
- Something they should change in their model and explain how this would improve their model.
- Ask a question about mechanism (the underlying cause and effect) in their model.

You will not submit this to D2L, but you should take notes on this. You must be prepared to share your feedback to the group with the whole class.

Model Revision

Based on the classroom discussion, make a revision to your model that improves your model's power to explain the phenomenon. You must revise your model in one of the ways listed below.

- Add something to your model and explain how this improves your model.
- Remove something from your model and explain how this improves your model.
- Change something in your model and explain how this improves your model.

Your group must submit your model and causal explanation as one document to the appropriate dropbox in D2L.

Bonus Challenge Question

Work on this any time your group finishes a part of the activity before the time for that activity has expired. If you complete the Challenge Question, submit your answer to the appropriate dropbox in D2L (titled Bonus)

Your body contains adult stem cells that are capable of proliferation and self-renewal. However, these cells typically do not divide until your body needs them. Based on your model and you knowledge of cell cycle checkpoints, predict the stage in the cell cycle in which you would typically find these cells. State an observation you could make on adult stem cells that would allow you to test this prediction.

Article Reference

"Stem Cell Basics." *Stem Cell Information.* NIH. 28 April 2009. Web. 26 Dec. 2012. <http://stemcells.nih.gov/info/basics/basics1.asp>.

Biotechnology Course: Modification

To Complete before Class:

- Review your outline on meiosis from Module 12 and you M3 and M6 models.
- Read sections 13.1, 13.2, 13.4 and 13.5 in the e-text.
- Watch the recording on models for selective breeding and mutation breeding.
- Explore the tutorial on making a genetically modified canola plant. http://ats.doit.wisc.edu/biology/g/bt/bt.htm
- Watch Two Videos on AquAdvantage Salmon
- http://www.youtube.com/watch?v=swYAuQjPnOc&feature=fvwrel
- http://www.youtube.com/watch?v=oyb3c9qbbK0
- Complete the Mastering Biology Homework
- Complete the outline.

Model Development

Your team will use the information from the readings, activities, recording, and homework to develop a model of genetic modification to make AquAdvantage salmon grow more quickly than unmodified Atlantic salmon.

1. Make a drawing that depicts a cell from a normal Atlantic salmon and a cell from an AquaAdvantage salmon. The model must include a causative explanation of how the genetic modification changes the salmon at the molecular level (monomers and polymers) and why this causes the salmon to grow more quickly. The causative mechanism should involve concepts related to genetic information (genes and promoters) and proteins and should incorporate key features from your M5 (redder protein), M8 (stem cell differentiation) and M18 (gene therapy) models as appropriate. You should clearly label the key features related to the causative mechanisms in the model.
2. Write a cause and effect explanation of how the genetic modification causes the salmon to grow more quickly that includes at least three linked cause and effect statements.

You should not submit this to D2L, but you must be prepared to present your model and explanation to the whole class.

Model Presentation and Feedback

As each group presents their model, think about how their model differed from your model. Concentrate on the features you labeled and the relationship between these features and the causal explanation. Think about how you might improve either their model or your model based on the differences. **Your feedback should include specific details to improve the model.** After the group finishes presenting their model, discuss in your group what feedback you might give that group to help them improve their model. Your feedback must include one of the following:

- Something they should add to their model and explain how this would improve their model.
- Something they should remove from their and explain how this would improve their model.
- Something they should change in their model and explain how this would improve their model.
- Ask a question about mechanism (the underlying cause and effect) in their model.

You will not submit this to D2L, but you should take notes on this. You must be prepared to share your feedback to the group with the whole class.

Model Revision

Based on the classroom discussion, make a revision to your model that improves your model's power to explain the phenomenon. You must revise your model in one of the ways listed below.

- Add something to your model and explain how this improves your model.
- Remove something from your model and explain how this improves your model.
- Change something in your model and explain how this improves your model.

Your group must submit your model including the depiction and cause and effect statements as one document to the appropriate dropbox in D2L.

If your team finishes early.

Your team will need to complete the team assignment. Use and extra time you have in class to organize your team and your team project. Requirements for the project are available in module 28 in D2L.

Cell and Molecular Biology Course: Ras in Cancer

Group Formation

Form a group of three students. At least one student in your group must have a Wi-Fi enabled device with which they can take a picture and upload the picture to D2L. Each student must log onto D2L individually and join group _____. To join the group, log on to D2L and choose this course. In a mobile browser you will need to choose "Desktop Version" at the bottom of the page. Join the group by clicking on the "Communications" tab on the top menu bar. Choose "Groups", pick the "Ras Signaling in Cancer" group, find your group number, and join the group.

Model Development

In this activity, your group will be developing a scientific model. This model, including all the drawings and explanations, must fit on the provided handout, should be constructed with the paper in landscape orientation, and must list your group number and group member names. You can either construct your model on paper or you can do so electronically if you can easily create freehand drawings on your device. If your group uses paper, you will need to take a picture of your model. Your group must submit your model electronically to the appropriate dropbox in D2L by 3:50. Find the "Ras Signaling in Cancer" dropbox in the "Model of Ras Signaling in Cancer" module. It will only appear after you have joined a group. Your group must also be prepared to present your model to the class.

You should use information from previous lectures, the textbook, your previous model of protein structure and function, and the article "Drug Strategy Blocks Leading Driver of Cancer" as you develop your model. Based on these materials you will be developing a model of how Ras works. Your model should illustrate: the structure-function relationship of Ras in normal cells; how the mutation that converted Ras from a proto-oncogene to an oncogene impacts the structure and function of Ras; and how the new drug impacts both normal Ras and mutant Ras.

1. Based on the scenario described at the top of columns 1 through 4, determine if signaling through the cell proliferation-signaling pathway will be active and what, if any, is the cellular response to those conditions. Write your answer in the appropriate spaces in the handout.
2. Develop structure-function models to explain what is happening with signal transduction in each scenario (columns 1 through 4). Your models should focus on the structure and function of Ras. Make drawings depicting your models in the appropriate spaces in the handout. Your model must include the following components.
    - Plasma Membrane
    - Receptor (any changes that occur with binding of the ligand should be illustrated)
    - Ligand (growth hormone) if appropriate
    - Ras structure (normal or mutant as appropriate)
    - GTP or GDP as appropriate
    - Drug if appropriate
3. In the appropriate spaces, write a cause and effect explanation using details from your model to explain what is causing the cellular response in that scenario. Each explanation should be one or two sentences and include the word "causes" or "because".
4. Prepare to present your model to the entire class if your group is selected.

Supplemental Materials

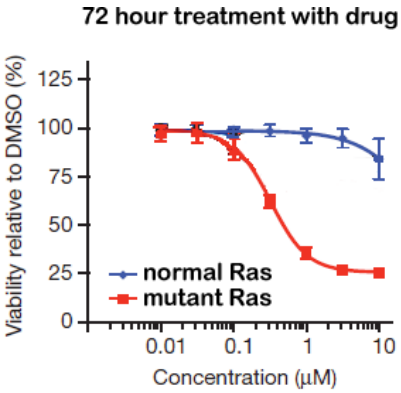
Model Presentation and Feedback

As each group presents their model, think about how their model differed from your model. Concentrate on the features you labeled and the relationship between these features and function. Think about how you might improve either their model or your model based on the differences. After the group finishes presenting their model, discuss in your group what feedback you might give that group to help them improve their model.

Model Predictions

Imagine an experiment where you grow cells in laboratory culture for each of the scenarios in your model. Imagine that you plan to count the number of cells produced at different time points for each experimental condition (using scenarios 1-4 as described above). At the bottom of this page, construct a graph predicting the number of cells that you think are likely to be measured in each culture vs time.

Model Evaluation



The graph to the right depicts results from an experiment that evaluated cell survival in the presence of the new drug. The X axis shows the concentration of the new drug that was applied to the cells. The Y axis shows the percentage of cells that were alive compared to cells treated with DMSO (the control treatment with no drug). Compared to cells treated with DMSO, what happens when cells with normal Ras are treated with the drug? Is this consistent with your model? If yes, explain why. If no, how might you modify your model to match these data? Compared to cells treated with DMSO, what happens when cells with mutant Ras are treated with the drug? Is this consistent with your model? If yes, explain why. If no, how might you modify your model to match these data?

Model Extension

Good scientific models address not only one specific phenomenon but help explain a range of related phenomena and make predictions about how currently unexplained phenomena might work. In this activity you developed a model that specifically explains how a new drug impacts Ras signaling in cancer. After you have complete your model, see if you can use your model to understand, explain, and make predictions about the related phenomenon listed below. If not, consider how you could revise your model so that it can be used to explain or make predictions about this phenomenon as well as the original phenomenon.

Trametinib is a drug that targets MEK, a protein kinase in the signal transduction cascade that is activated by Ras. Can you use your model to predict how Trametinib works? What parts of your model are relevant to both Trametinib and the new drug that targets Ras? What parts of you model are only relevant for the new drug that targets Ras and not to Trametinib?

Article Reference

University of California - San Francisco. "Drug strategy blocks leading driver of cancer." ScienceDaily. ScienceDaily, 20 November 2013. <www.sciencedaily.com/releases/2013/11/131120133735.htm>.

Model Scaffold

	Column 1 Normal Cell: G_0	Column 2 Normal Cell: moving into S	Column 3 Cancer Cell: Mutant Ras; no drug	Column 4 Cancer cell: mutant Ras; new drug
Active signal transduction?				
Cellular response?				
Model Required components: • Plasma Membrane • Receptor • Ligand (growth hormone) if appropriate • Ras structure (normal or mutant as appropriate) • GTP or GDP as appropriate • Drug if appropriate				
Cause and Effect Explanation (1 or 2 sentences)				
Group #_____ Names 1. 2. 3.				

Cell and Molecular Biology Course: Specialization

Group Formation

Form a group of three students. At least one student in your group must have a Wi-Fi enabled device with which they can take a picture and upload the picture to D2L. Each student must log onto D2L individually and join group _____. To join the group, log on to D2L and choose this course. In a mobile browser you will need to choose "Desktop Version" at the bottom of the page. Join the group by clicking on the "Communications" tab on the top menu bar. Choose "Groups", pick the "Stem Cell Differentiation" group, find your group number, and join the group.

Model Development

In this activity your group will be developing a scientific model. This model, including all the drawings and explanations, must fit on one piece of paper and should be constructed using the paper scaffold provided in class. You can either construct your model on paper or you can do so electronically if you can easily create freehand drawings on your device. If your group uses paper, you will need to take a picture of your model. Your group must submit your model electronically to the appropriate dropbox in D2L by 3:50. Find the "Stem Cell Differentiation" dropbox in the "Stem Cell Differentiation Modeling" module. It will only appear after you have joined your group. Your group must also be prepared to present your model to the class.

The purpose of this model is to explain the molecular similarities and differences between an unspecialized stem cell, an eye cell, and a heart cell.

1. On the scaffold you are given a representation of the **same portion of the genome** from these three different cells. Each box on the genome represents an enhancer (E), promoter (P) and gene (G). Use what you have learned about the central dogma, protein structure and function, regulation of gene expression, and stem cells, to add details to this representation that explain the similarities and difference between these cells at the molecular level (the level of monomers and polymers). The following details must be represented in your model:
    a) The function of the protein encoded by each gene. Make up the functions based on a types of protein you think would be required to make each type of cell.
    b) The sequence found in the enhancers and promoters in each cell. Note that in real cells, enhancers, promoters and genes can be 100s or 1000s of nucleotides in length. You only need to depict enough nucleotides to allow you to explain the similarities and differences between the cells. You can make up these sequences as the actual sequence isn't that important here, we want you to focus on the similarities and differences between these sequences.
    c) The sequence found in mRNA produced in each cell.
    d) The primary and tertiary structure of protein produced in each cell.
    e) The cause, at the molecular level, of the differences between the cells.
2. Write a statement describing the similarities and differences between the cells and a **cause and effect** explanation of why the cells are different and what causes those differences to come about. The explanation should incorporate concepts related to monomers, polymers, information in the DNA, regulation of gene expression, and proteins.

3. When your model is complete, swap with a neighboring group. Each group should evaluate the other group's model and have a discussion with the other group giving them constructive feedback about the *scientific merit* of the other group's model. Be sure to include one strength of the other model and one area where the other model could be improved. After this discussion fill out the space labeled #3 on your own model describing your interpretation of the feedback from the neighboring group. Include how you might improve your model based on the other group's suggestions. It is your choice to modify your model or not based on this feedback.
4. Prepare to present your model to the entire class if your group is selected.

Supplemental Materials

Challenge Questions

If you finish early, work on these challenge questions.

Use your model to predict the outcomes for each of the following situations. If you model cannot predict the outcomes, you should modify your model.

- You sequence all the DNA in each of the cells and compare the sequences. What do you find?
- You sequence all the mRNA in each of the cells and compare the sequences. What do you find?
- You sequence all of the proteins in each of the cells and compare the sequences. What do you find?

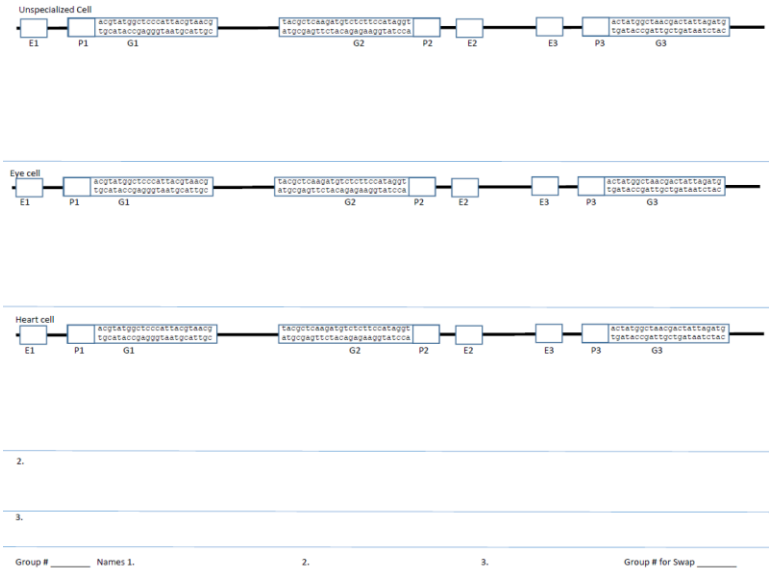
Based on your model, predict how changing the DNA in a promoter in a gene important for stem cell differentiation could impact the process of differentiation. Based on your model, predict how changing the DNA in an enhancer in a gene important for stem cell differentiation could impact the process of differentiation. Explain you prediction using your model. Your explanation must include the concept of monomers and polymers and information. State an observation you could make using stem cells that would allow you to test this prediction.

References

"Stem Cell Basics." *Stem Cell Information.* NIH. 28 April 2009. Web. 26 Dec. 2012. <http://stemcells.nih.gov/info/basics/basics1.asp>.

Ludwig-Maximilians-Universitaet Muenchen. "Stem-cell Research: A New Genetic Switching Element. *ScienceDaily*. ScienceDaily, 22 May 2014. <http://www.sciencedaily.com/releases/2014/05/140522104854.htm>.

Model Scaffold



Supplemental Materials

Supplement 2. Interview protocol **(**for topics 4-7, main questions are in **bold** and possible follow-up questions are bulleted**).**

1. Introduction

Hi, [Student's name], my name is Dr. Andrea Bierema. I am a researcher in science education here at MSU. In your biology class last semester, BS 161, you completed several modeling activities. During the semester, we recorded your [list modeling activities]. We are talking with a few students, like you, to help us learn more about what you learned and what you thought of the modeling activities. For this interview we will focus on the [Ras Signaling or Stem Cell Differentiation] model. Thank you very much for agreeing to talk with me. The interview will last anywhere from 15 to 30 minutes.

2. Interview Process

Before we begin discussing the models, I just have a few notes to go over with you regarding the interview process.

- We will be talking today about your ideas regarding the models you constructed,
- There are no right or wrong answers,
- Your answers will not affect your GPA in any way,
- You will receive $10 Spartan Cash for this interview and I will need to collect your PID number in order to tie the $10 to your PID,
- If you are uncomfortable in any way we can stop,
- I am going to record the interview because I am interested in your ideas and want to be sure that I have a good record of everything you say,
- I want to let you know that we may share some of your ideas with teachers and researchers who are interested in students' ideas about modeling, but your name will not be connected with your ideas or models in any way,
- Since the models were created last semester, it is completely acceptable not to remember every detail regarding the model. Just try your best to remember and let me know if there is anything that you are uncertain about.

Before starting the interview, please sign this consent form. It is similar to the one that you saw in class, but it includes the interview portion of this study.

3. Student Questions

Before we begin, do you have any questions about the interview?

4. What the Model Explains

First, what did you want your model to show (what were you trying to explain)?

- *Ras Signaling Model*: (Mechanism) How does your model explain how Ras signaling works in normal cells and mutated cells? How does your model explain how a new drug impacts Ras signaling in cancer?
- *Stem Cell Differentiation*: (Mechanism) How does your model explain the molecular similarities and differences between an unspecialized stem cell, an eye cell, and a heart cell
- What do these [words, numbers, symbols] represent in your drawing? Why did you use them?
- What are the most important parts of your model? Why?
- What are the less important parts of your model? Why?
- (Evidence) What have you seen or heard (in your life or in class) that makes you think this happens? **(Audience) Who is the model for?**
- Why—say more? How might……use this model?

- Is the model useful for anyone else?

5. *Model Revisions*

From the recording, we were able to obtain drafted models that were created during the activity. I would like to discuss why the revisions occurred. Let's look at this change first. Why was this change made? [go over more than one change, if necessary]

- You mentioned that the model was for …… Why do you think … would have preferred the model this way than the way you had it before?
- *Ras Signaling Model*: How did this change help you better explain how Ras signaling works in normal cells and mutated cells and how a drug impacts Ras signaling in cancer?
- *Ras Signaling Model:* Why did you change the model after writing the cause and effect explanation?
- *Ras Signaling Model:* After working through the instructions from "Model Predictions"/"Model Evaluation"/"Model Extension" section, why did you change the model? How did these changes help your model?
- *Stem Cell Differentiation*: How did this change help you better explain the molecular similarities and differences between an unspecialized stem cell, an eye cell, and a heart cell?
- *Stem Cell Differentiation:* Why did you change the model after writing the explanation of similarities/differences and cause and effect?
- *Stem Cell Differentiation*: Why did you or why did you not make changes after looking at another group's model?
- *Stem Cell Differentiation:* Why did you make changes after working on the Challenge Questions?

If you could change your model now, what would you do? Why?

6. *Model Consensus*

What was the process of working in a group to develop and revise a model like? How do you think your group worked together as a team? What happened if you disagreed? How did you resolve any disagreements? How did you contribute to the production of the model?

- *If the Drawer*: Were there parts that you were unsure about as you created the model? Did you always ask your group for feedback?
- *If Not a Drawer*: How often did you provide feedback to the drawer? Did you bring up any ideas without being asked by the drawer?
- Did you agree with all of the components and how the components were represented?
- If you were working on this model independently, is there anything that you would have done differently? Why? Why were these changes not made in the final model?

7. *Reflection*

What do you believe was the purpose of these model activities? What do you believe was the purpose of doing these model activities in a group instead of individually?

- What were the most and least helpful parts of creating these models?
- How did they help or hinder learning about the material and how to do science?
- Did they help in preparing for the exams?
- If you could have changed anything in the original worksheet(s) that you completed, what would you change?
- Have you done similar activities in a previous science course (either college or high school)?
- If given the option, would you want to do similar model activities in another science class?

Do you think participating in this study impacted your group's ability to create the model?

- How did you feel about creating the model on a Surface Pro tablet?
- Were there any issues with the software?
- Why did you volunteer to participate during this/these modeling activities, but not the other modeling activities?

8. *Conclusion of Interview*

[Student name], thank you for sharing your ideas. I enjoyed very much hearing your thoughts about science and science learning. Do you have any questions you would like to ask me before we finish?