

## **Descriptions and legends for supplemental materials**

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**S1: Overview of goals and activities in the authentic research module**

<b>Authentic research module to answer the question:</b> What is the effect of overexpression of a DNA replication licensing gene in the single celled organism, <i>Tetrahymena thermophila</i> ?			
	<b>Week 1</b>	<b>Week 2</b>	<b>Week 3</b>
<b>Learning goal</b>	Students can use gene structure and the Central Dogma to discuss conservation and mutation.	Students can identify limitations of existing data and use new laboratory techniques to identify ways to test hypotheses.	Students can use prior content and technical knowledge to refine and test a hypothesis.
<b>Pre-laboratory work/prior knowledge</b>	Students revisit the basic tenets of the Central Dogma and DNA replication control.	Students examine previous data related to the overexpression of CDT1, a protein that regulates DNA replication.	Students refine previously generated hypotheses into testable hypotheses regarding the role of CDT1 in a cell.
<b>Laboratory activity</b>	Students use bioinformatic analysis to explore genes involved in DNA replication	Practice with phenotypic assays (microscopy of living or fixed cells, cell counts, nuclear staining, image capture and analysis).	Comparison of wild type and Cdt1 overexpressing cells using phenotypic assays learned the week before.
<b>Out of class activity</b>	Worksheet on the role of genes and proteins in DNA replication and preliminary hypothesis about the cellular impacts of over- or under-expression of CDT1	Worksheet to narrow down choices of experimental tools and refine hypotheses.	Final write up of whole-class and individual data sets as two annotated and captioned figures with an associated explanatory paragraph.

**S2:** Description of the research module on cell cycle control in *Tetrahymena thermophila* (A detailed description and protocols is available elsewhere [in revision, CourseSource]).

The laboratory research module addressed the fundamental cell biological question of how the cell cycle is regulated (Table 1). The module and associated manual is more thoroughly described elsewhere (CourseSource, in revision). The module presented students with an opportunity to apply prior skills and knowledge to investigate a research problem using a model biological system, the single-cell ciliate model organism, *Tetrahymena thermophila*. The *Tetrahymena* strain that we used can overexpress the protein CDT1 fused to Yellow Fluorescent Protein (YFP). Because CDT1 is required for licensing (identifying and initiating polymerization at) origins of DNA replication, it is likely to play a central role in cell-cycle control in *Tetrahymena*.

Prior to the three-week research module, all students worked through a series of traditional laboratory exercises that introduced them to pipetting and dilutions, light microscopy techniques, model organisms (including *Tetrahymena*) and their uses and advantages, and simple protein biochemistry. The research module followed an interactive lecture on Molecular Biology in the classroom. All laboratory sessions began with a Prelab presentation (given as a PowerPoint slideshow) and discussion (prompted by phrases, questions, or data in the PowerPoint) led by the lab section graduate teaching assistant (GTA). Students worked as pairs in the laboratory and their laboratory work was followed by a post-lab activity or homework completed outside of class.

In the first week of the research module, students worked in pairs to gather publicly available information about four genes (CDT1, MCM2, ORC6, and GEMININ), and analyzed their sequences using online bioinformatic tools. In order to motivate discussions on why students might be interested in studying these genes, human disease associated variants were included in this exercise (Bicknell et al., 2011a, 2011b; Burrage et al., 2015; de Munnik et al., 2015). Next, students integrated this information with what they had already encountered in lecture and engaged in a guided discussion that explored why a model organism might be useful for studying these genes, which are conserved across Eukarya. Students generated initial hypotheses about the impact of particular gene perturbations (such as overexpression or mutation) on the physiology of a model organism, and critically evaluated existing data for strengths and weaknesses.

In the second week of the lab, students learned various simple phenotypic assays (cell counting using hemacytometers, microscopy on living and fixed cells, image acquisition and

analysis) and used their understanding of these tools to further refine their initial hypotheses into testable ones. Students were introduced to the research question, in part, by analyzing preliminary data obtained by an undergraduate student in a semester-long CURE at Washington University in St. Louis, which can be found at [suprdb.org/index.php/searchDetails/geneName/cdt1](http://suprdb.org/index.php/searchDetails/geneName/cdt1).

In the third week of lab, students honed a testable hypothesis, chose tools with which to test it, and implemented their experimental plan. They gathered data on the growth and morphology of wild type and mutant cells. Data from pairs of students was collected from all of the lab sections that were participating in the research module, and was compiled for statistical analysis. Students were asked to evaluate their data and the class' data in the form of a scientific figure and caption.

Students were provided with a model system (*Tetrahymena thermophila* strains with or without the Cdt1:YFP transgene), the name and sequence of a candidate gene (Cdt1), and training in several techniques to enable qualitative and quantitative observations. The three week module followed the structure outlined in S1; the traditional laboratory sessions during the same weeks were DNA Sequence Analysis (Week 7), Mitosis in Garlic Root Tip Cells (Week 8), and Exploration of Photosynthesis (Week 9). Figure 1 shows an overview of how the laboratory and classroom sessions align with the assessments that are described in this manuscript.

#### Works cited

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- Bicknell, L.S., Walker, S., Klingseisen, A., Stiff, T., Leitch, A., Kerzendorfer, C., Martin, C.-A., Yeyati, P., Al Sanna, N., Bober, M., et al. (2011b). Mutations in ORC1, encoding the largest subunit of the origin recognition complex, cause microcephalic primordial dwarfism resembling Meier-Gorlin syndrome. *Nat. Genet.* **43**, 350–355.
- Burrage, L.C., Charng, W.-L., Eldomery, M.K., Willer, J.R., Davis, E.E., Lugtenberg, D., Zhu, W., Leduc, M.S., Akdemir, Z.C., Azamian, M., et al. (2015). De Novo GMNN Mutations Cause Autosomal-Dominant Primordial Dwarfism Associated with Meier-Gorlin Syndrome. *Am. J. Hum. Genet.* **97**, 904–913.
- De Munnik, S.A., Hoefsloot, E.H., Roukema, J., Schoots, J., Knoers, N.V., Brunner, H.G., Jackson, A.P., and Bongers, E.M. (2015). Meier-Gorlin syndrome. *Orphanet J. Rare Dis.* **10**.

### S3: Metacognitive prompts and their use in the authentic research module.

Outline of the authentic research module (left) and associated metacognitive prompts (right). Students were prompted by instructors, in-class lecture slides, and take-home worksheets to reflect on the activities they participated in, as well as on their own thinking, before, during, and after their laboratory sessions.

#### Outline of Laboratory Module

**Week 7:**

Students use bioinformatic analysis to explore genes involved in DNA replication

**Objective:**

- Use bioinformatics tools to investigate gene structure, DNA replication genes, mutant alleles, and model organism (*Tetrahymena thermophila*) homologs.

**Week 8:**

Students practice phenotypic assays: Counting, staining, imaging, and measuring *Tetrahymena* cells and organelles

**Objectives:**

- Students can identify limitations of existing data
- Generate initial hypotheses for Cdt1 o/e.
- Use previously learned skills to gather data in a new system.
- Learn new laboratory techniques for data collection, and to identify ways to test an hypotheses.

**Week 9:**

Comparison of wild type and Cdt1 overexpressing cells using assays learned in Week 8.

**Objectives:**

- Use prior content and technical knowledge to refine and test an hypothesis.
- Define research question.
- Refine initial hypotheses to be testable.
- Design a protocol based on available tools.
- Gather data to test a hypothesis.

**Week 10:**

Individual analysis of individual's data

**Objectives:**

- Display, explain, and critique individual and group data using graphical and statistical analysis.

#### Representative Metacognitive Prompts

- Where have you seen these genes before?
- How might the mutation affect the function of the protein? What makes you think that?
- What bioinformatics tools were the easiest for you to use? Which ones gave you the most useful information?
- Why might you want to study this gene using a model organism rather than human subjects?

- What do you remember about CDT1 and its function in the cell cycle?
- What are the strengths and shortcomings of previous studies?
- What prior knowledge did you use to form your *initial* hypothesis?
- Which of the experimental tools you've learned in this course could you use to test your hypothesis?
- How confident are you in your answer for the questions above? What would make you more confident?

- What is a *testable* hypothesis for your research question?
- What prior knowledge did you use to come up with your *testable* hypothesis?
- What tools will you use to test your hypothesis? Why did you choose these?
- What will you do if something doesn't work well?
- How will you know if your methods are working?

- Was your hypothesis supported or rejected? Explain your reasoning.
- Why does the N of measurements matter?
- What conclusions can you draw from this data? Are you confident in your conclusions? Why or why not?
- How does your data compare to the class' data? What explains similarities or differences?

#### **S4: Task-based question**

The following is the task-based question that was administered to students for extra credit as part of their laboratory practical exam. It was designed to elicit responses that require self-direction and self-reflection in a laboratory context. Student responses were transcribed and coded as described in the Methods section.

*Robin has been counting fixed cells in 3 different samples using a hemocytometer and has been getting some confusing results. Robin has counted each sample 3 times, using the four different quadrants of the hemocytometer, as described in her lab manual. Although her average cell counts suggest that some of her samples have more cells than others, some of her individual replicates have many fewer cells than other replicates. Robin's protocol was written so that she would follow the same procedure each time she counted the cells, but there are a few notes in her manual suggesting that some of her samples might have been treated differently over the course of the lab session. In a previous lab session, Robin had gotten very consistent cell-count data while working with her lab partner, Suzanne. They had counted cells for a "dry run" to make sure that all of their equipment was working properly, but those cells are no longer available. How should Robin think about planning her next step(s)?*

**S5:** Set of coded answers to a task-based question.

These coded answers were used to analyze student responses to the task-based question (S4); responses were coded into the following categories by statement.

<b>Code #:</b>	<b>Name:</b>	<b>Complexity:</b>	<b>Description:</b>
1	Ask instructor/Grade focused	Simple	Robin is instructed to ask the TA or professor what to do next and/or how to fulfill the assignment
2	Accept data and move on	Simple	No action or changes suggested before continuing the experiment/lab
3	Follow/consult lab manual	Simple	Robin is instructed to consult the lab manual either to continue her work or to decide/discover what she might have done wrong
4	Write up what happened	Simple	No changes or actions are suggested, but Robin is told to write down what happened and/or note her concerns about the data/results
5	Clean cover and plate with ethanol	Simple	Robin should be sure the results are accurate by cleaning the cover and plate with ethanol
6	Redo experiment	Simple	Robin should start over, redo her samples, or take new samples.
7	Recount or recalculate	Simple	Robin should check her totals by recounting her cells and/or recalculating her averages
8	Ask classmate for help	Simple	Robin should ask her lab partner or another classmate about what to do
9	Figure out why results, what errors	Medium	Robin should find out why her data are unexpected
10	Compare/do separate treatments separately	Medium	Robin should improve consistency by separating the process and/or samples of the different treatments by space and/or time

11	Use dry run data	Medium	Robin should use the data she got on her dry run instead of the "official" baseline samples
12	Consider controls/consistency	Complex	Robin should make sure that her work is consistent and control for differences across samples
13	Address sampling bias/method	Complex	Robin should try to avoid outlier results by using consistent samples.
14	Add/compare to others' experiments/data	Complex	Robin is instructed to compare her results to others' to see if they are similar, or to not worry because it'll be combined with the class data.
15	Do more replicates/samples	Simple	Robin should get more data points
16	Validate baseline and/or data variability	Complex	Robin should establish what kind of variation in data/results is common and/or usable
17	Check calibration/recalibrate	Simple	Robin should check the calibration or recalibrate, or increase the amount of times she checks or recalibrate between readings
18	Control light/time on tubes	Medium	Robin should make sure the intensity and/or time of the samples' light exposure is consistent
19	Speed up/do it fast	Medium	Robin should increase her speed or make sure she's fast enough
20	Control solution concentration	Complex	Robin should consider the components and even suspension/mixture of her solution
21	Control pipetting	Medium	Robin should make sure she is pipetting consistently/correctly
22	Increase detail/precision for own instructions/procedure	Medium	Robin should increase her consistency by being more detailed or specific as she plans doing her experiment



23	Use slopes not intercepts to calculate rate	Complex	Robin should make her data answer the research question by using only the relevant values in her calculations (slopes) and working around the irrelevant (intercepts)
24	Linear results; compensate for initial absolute difference	Complex	Robin should make a mathematical correction to account for details of the experiment.
25	“Robin could look at the plates to see if the colonies formed more densely in one corner of the plates. She could also check with the wild type plate to see if any of the bacteria was defective. Robin might also create an enzyme pathway to figure out what substrates are causing/impeding growth.”	Complex	One time answer, exact words

**S6: Pre-post survey questions.**

#	Question
1	When studying biology, I relate new information to what I already know rather than memorizing it the way it is presented.
2	If I understand a biological system, I can make a prediction about how changing a variable would affect that system.
3	Knowledge in Biology comes from the results of experiments.**
4	When I am introduced to a topic or idea in Biology, I think about what parts are already familiar to me, and why they are familiar to me.**
5	Biology is primarily about learning known facts as opposed to investigating the unknown.*
6	When I am describing a biological process, I find it difficult to put what I know into my own words.*
7	Finding out what you do not know about a biological process is as important as what you do know.
8	To identify what exactly I don't understand about a particular subject, I first try to determine what I do know.
9	There are times I think about or solve a biology question in more than one way to help my understanding.*
10	I think about biological questions in terms of how I could test a hypothesis.
11	Developing testable hypotheses is an important part of science.
12	There is usually only one correct approach for testing a hypothesis.*
13	I can make a simple diagram that provides an overview of an experiment.
14	How an experiment is designed can determine if the experiment runs successfully.
15	I understand why experiments have controls.
16	If two different groups of scientists study the same question, they will likely come to similar conclusions.
17	If different individuals obtain different results, no conclusions can be made.
18	Mathematical skills are important for understanding biology.*
19	A conclusion is strengthened if an experiment gives the same result when it is repeated by more than one individual.
20	If an experiment does not give the expected outcome for the hypothesis, then you can't learn anything about that hypothesis.
21	The material in Bio205 is frustrating to understand.
22	My understanding of biological systems is enhanced by connecting material learned in class to material in my textbook.**
23	I get a sense of enjoyment in the process I use in Biology 205 laboratory experiments.
24	I am confident in my ability to understand the material being taught in Biology 205.
25	Who is your instructor for Biology 205?
26	What is your major or intended major?

\* C-LASS with little or no change in language      \*\* C-LASS with moderate change in language

Questions 1-24 were presented in groups of 4 and 5 per page, and were preceded by the sentence: "Please choose the answer that most accurately reflects your feeling about the following statements." The answer options for questions 1-23 were:

*Strongly agree, somewhat agree, neither agree nor disagree, somewhat disagree, or strongly disagree.*

For questions 25 and 26, students were given space to fill in their expected major or were provided with a drop down menu to choose their instructor.