Lesson Plan

Title
Where There's a Worm There's a Way: Exploring Molecular Genetics with *C. elegans* and RNAi
Primary Subject Area
Biology
Grade Level
10-12
Overview
Gene expression is an integral piece in understanding the transmission of genetic information in living things. In this activity, students will use RNAi in the model organism *C. elegans* to explore the central dogma and its relationship to mutations and phenotype.
Approximate Duration
Two days (plus lab preparation time)
Massachusetts Frameworks
3.2 Describe the basic process of DNA replication and how it relates to the transmission and conservation of the genetic code. Explain the basic processes of transcription and translation, and how they result in the expression of genes. Distinguish among the end products of replication, transcription, and translation. 3.3 Explain how mutations in the DNA sequence of a gene may or may not result in phenotypic change in an organism. Explain how mutations in gametes may result in phenotypic changes in offspring. SIS1. Make observations, raise questions, and formulate hypotheses. SIS2. Design and conduct scientific investigations. SIS3. Analyze and interpret results of scientific investigations. SIS4. Communicate and apply the results of scientific investigation
Interdisciplinary Connections
- Students may be interested in the history of the use of *C. elegans* as a model organism and the emergence of molecular biology in the 1960s. Have students research Sydney Brenner and his Nobel Prize in Medicine for more information. - Students may be familiar with controversy in the media regarding public funding of scientific research. Have students research the National Science Foundation and the funding of basic research projects. Have students defend and debate the funding of projects involving *C. elegans* and other topics with which the public has little familiarity.
Lesson Objectives
At the end of this lesson, students will be able to: • Trace the flow of genetic information from gene to protein. • Explain how RNAi can disrupt gene expression. • Relate mutations in genotype to observable phenotypes. • Describe the utility of *C. elegans* as a model organism in studying genetics.
Lesson Materials and Resources
There is a kit from Carolina Biological (Item #211391 "Introducing RNAi by Feeding Kit" with prepaid coupon for living organisms, $149.00) that includes most of the materials necessary to run this lab. I would suggest purchasing this kit and supplementing it with the materials listed below:

- Metal spatula
- Incubators at 37℃ and 20℃
- Refrigerator
- Dissecting microscopes
- PowerPoint file (attached)
- Observation/lab sheet (attached)

Technology Tools and Materials

Throughout the course of this activity students will have the opportunity to practice using the following tools:

- Dissecting Microscope

Background Information

Since its first documented use as a model genetics organism by Sydney Brenner in 1963, *C. elegans* has become one of the most widely used organisms for genetic study. In fact, many of the characteristics that make this nematode appealing to research scientists can also apply to the high school biology laboratory. It is often described as an animal that acts like a microorganism--inexpensive and easy to raise in just a few days, transparent so the organs are visible under classroom microscopes, and self-fertilizing with many offspring. Strains are readily available from a number of sources.

The worms are particularly useful for genetic manipulation studies, and a “quick and easy” method is through the use of RNA interference, or RNAi. Through this procedure we can "feed" the worms double-stranded RNA (dsRNA) via a plasmid transformed in *E. coli*. When the worms eat the bacteria, the dsRNA destroys the mRNA transcript produced during protein synthesis. As a result, we can hatch a generation of worms missing an entire gene or protein, and observe the phenotype that results. In *C. elegans*, this entire process can occur in just one week. Carolina Biological offers a kit that contains most of the materials necessary to perform RNAi experiments in the worms, and the results can be applied to numerous areas of the traditional high school biology curriculum, notably topics in molecular genetics.

Lesson Procedures

Teacher Preparation:

- Follow the specific instructions in the Carolina kit for preparing the worms and *E. coli*.

Student Lesson:

Day 1:

- Introduce the lesson with the “Intro to *C. elegans*“ portion of the PowerPoint. (10 mins)
- Split student into groups to observe the wild-type worms. They should use their lab sheets (Day 1, Part 1) to record observations. (20 mins)
- Bring the class back together to discuss observations. Relate observations of specific phenotypes back to the concept of gene expression and the flow of genetic information. Use these questions to guide the discussion: (15 mins)

1. What did you observe? How did the worms behave? How did they move? Did they interact with other worms? Did you see any males? Was it hard to focus on one worm?
2. How does phenotype relate to genotype? Reference both morphology and behaviors of the worms when discussing phenotypes.
3. What would happen if gene expression were disrupted, and how this might affect the worm at both the genotype and phenotype level? Talk about mutations, transcription and translation.
4. Tomorrow we will observe worms that have had gene expression disrupted. On your lab sheet (Day 1, Part 2), read about each mutant phenotype and propose a hypothesis about how these worms will compare to the wild-type worms you saw today.

Day 2:

- Students should split back into their lab groups to observe the RNAi-silenced worms and compare the results to their hypotheses. They should record observations on their lab sheets. (20 mins)
- Bring the class back together to discuss observations and relate to yesterday's discussion. Discuss the process of RNAi using the "RNAi" portion of the PowerPoint, and relate it to gene expression in worms. Show the phenotype video clips to wrap-up. (25 mins)
- For homework, have student complete the analysis questions on their lab sheets.

Assessment Procedures

Students must turn in their completed lab sheets with observations, hypotheses and analysis questions answered. In addition, material related to this lab activity and objectives will appear on the unit test.

Accommodations/Modifications

If the topic of RNA interference is too complicated for the level of your students, you can modify the lesson to focus just on the concept of genotype vs. phenotype as students observe the various phenotypes of both the wild-type and mutant worms.

Reproducible Materials

Lab sheets are attached. Teachers may also wish to distribute copies of the PowerPoint.

Explorations and Extensions

Students could perform the RNAi on their own if they have sufficient time or preparation. This might be a particularly good extension for AP students, and complete instructions are provided in the Carolina kit materials. You can also order mutant worms with each of these phenotypes from Carolina for comparison.

Lesson Development Resources

- PowerPoint modified from Dr. Erin Cram (Northeastern University)
- Lab procedures modified from Dr. Erin Cram (Northeastern University), Melissa LaBonty (Northeastern University) and "Introducing RNAi by Feeding Kit" (Carolina Biological #211391)
- Background information from *Anal Biochem*. 2006 Dec 1;359(1):1-17. *A biochemist's guide to Caenorhabditis elegans*. Corsi AK.

Additional *C. elegans* Resources:

- My RET Site: romanoret.weebly.com
- WormBase: www.wormbase.org
- WormBook: www.wormbook.org
- WormAtlas: www.wormatlas.org
- Wormimage: www.wormimage.org
- WormClassroom: www.wormclassroom.org

Reflections

I have found that through performing an "egg prep" you can synchronize the hatching times of the worms on the seeded plates. Though the procedure is more detailed than the Carolina procedure, it yields much better results. Alternately, the *talin* gene yields a very obvious phenotype. Please contact me for details.

Contact Information

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