

In Sickness and in Health: Understanding Familial Disease Inheritance and Personalized Medicine Through Genomics.

This activity series focuses on the central dogma of molecular biology to consider the concept of health and disease from the DNA level. Students will conduct an interactive case study of a disease-causing genetic mutation, use Legos to illustrate transcription/ translation and create an original piece of art that depicts an interviewed scientist's research.

Activity courtesy of HOPES 2013 Recipients

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Teacher

Quick Guide and Materials:

- **Age Range:** High School
- **Preparation Time:** ~ 2 hours
- **In Class Time:** ~ 4 hours
- **Duration:** >4 weeks
- **Materials List:** Legos, Art Supplies, Computer with Internet Access

www.asbmb.org/912activity/sql



Sample Activity Outline and Preparation

Activity Outline

| Class.Sequence | Activity | Timing | |
|--------------------------|----------|--|--------------|
| Activity Breakdown Below | 1.1 | Lecture- Organisms to DNA: Organization of Biology | 30 min |
| | 1.2 | Review an Example Case Study | 15 min |
| | 1.3 | Assign Case Studies to Groups | 5-10 min |
| | 2 | Case Study Presentations | 10 min/group |
| | 3.1 | Lecture- Central Dogma of Molecular Biology | 20 min |
| | 3.2 | Lego Activity | 30 min |
| | 3.3 | Guidelines to “Interview a Scientist” | 5-10 min |
| | 4 | Art Project | 60 min |

Preparation

1. Review existing lecture materials, or create new.
2. Obtain legos: need ~300 1x1 Legos @ \$0.10/Lego at shop.lego.com (colors described below)
3. Use network to locate potential scientists to interview
4. Source art materials: Canvas, whiteboard, paint, colored pencils, etc.

National Science Education Standards

Life Sciences

The cell – C1c. – Cells store and use information to guide their functions. The genetic information stored in DNA is used to direct the synthesis of the thousands of proteins that each cell requires.

Science as Inquiry

Abilities necessary for apt scientific inquiry – A1c. – Use technology and mathematics to improve investigations and communications.

Abilities necessary to do scientific inquiry – A1d. – Formulate and revise scientific explanations and models using logic and evidence.

Understandings about scientific inquiry – A2d. – Mathematics is essential in scientific inquiry. Mathematical tools and models guide and improve the posing of questions, gathering data, constructing explanations and communicating results.

Science and Personal and Familial Perspectives

Personal and community health – F1c. – Personal choice concerning fitness and health involves multiple factors. Personal goals, peer and social pressures, ethnic and religious beliefs, and understanding of biological consequences can all influence decision about health practices.

Week One and Two

Lecture Material

Lecture- Organisms to DNA: Organization of Biology

The lecture is to describe the biological composition of an organism, and how information in DNA works to create the organism. The lecture covers rules that define an organism, organizational hierarchy (organs, tissues, cells, etc), and introduces DNA, proteins, and genetics.

Example is found at: http://prezi.com/entowokn86ap/overview-of-organisms-molecular-biology-and-dna/#share_embed

Case Study

Scenario for students: The bioinformatics researchers (computer scientists) at the clinic have analyzed the genome of a current patient, and they have just returned the DNA mutation in a gene most responsible for the patient's condition. The task is to use the gene and DNA mutation information they have provided to identify the disorder the patient has.

DNA - Gene (information) - Proteins - Cells - Tissues - Organs - Organisms

The critical pieces we are considering today are the genes and proteins. The goal is to explore how diseases are linked to genetics. Each group will present their findings during class in a 10 minute presentation.

Group Case Study Assignments:

Cardiovascular Disease Group - PCSK9: Patient is average height and build, and has worked at a computer for 10-12 hours a day for the past 28 years. After work the patient immediately heads home to read, watch movies, or play video games until it's time for bed.

Oncology (Cancer) Disease Group (tp53/BRCA1): Patient has smoked 8-10 cigarettes a day since they started smoking high school. They are now 34. They have expressed to doctors that they sometimes have trouble breathing in high altitudes i.e. when they go on the annual family ski trip.

Regulatory Disease Group (TCF7L2): The patient consumes most of their liquids from starbuck which include concentrated juices and coffee beverages. On average the patient has had 2 a day for the past 15 years. The patients primary diet consists processed and microwavable foods because they are easiest for a quick lifestyle. The patient is a successful business person who is traveling most of the time in and out of airports.

Neurological Disease Group (APOE4): Since graduating college this patient has discontinued using the study habits which made them successful. In clinical examination they cannot remember the last time they read a novel of significant length. *If APOE4 searches are confusing just try APOE.

Pulmonary Disease Group (CFTR): Since turning 13 the patient has had numerous infections with pneumonia and bronchitis all within the same year. The child is often coughing and has no known allergies.

Questions to answer in presentation:

1. Describe the function of your gene. How do mutations affect it? (www.genecards.org)
2. Based on the function of the gene/protein, how does it contribute to illness/death. Think of organs it may affect, or its biological role. (<http://www.mayoclinic.com/health/>)
3. What is a daily lifestyle plan that addresses/prevents/reverses specific illness features? This question may be difficult to explain, but please make an attempt.
4. How does the lifestyle and health plan address specific genetic or physical features of the disease?
5. Do any medicines or therapies exist to treat this disease?
6. Identify any aspects of this condition that could benefit from increased medical research? Can you identify an aspect of this disease that is not well understood?
7. Identify a famous person, or member of popular culture, who suffers from this disease? If this is not possible think of or a similar condition, or a condition that affects a similar organ. Demonstrate how their life has been affected by the condition.

Example Case Study: ID Gene: PKD I

Describe the function of the gene: Polycystin-I is a glycoprotein. It may function as an integral membrane protein involved in cell-cell/matrix interactions, and may modulate intracellular calcium homeostasis and other signal-transduction pathways. It plays a role in renal tubular development, and mutations in this gene have been associated with autosomal dominant polycystic kidney disease. Renal tubules are responsible for filtering fluid in the kidney.

How does it contribute to illness/death? This disease would cause the kidneys to not function. Have one kidney properly working could potentially be ok, but once both kidneys fail to function the patient would progress to a critically ill state.

What is the daily plan that addresses/prevents/reverses specific illness features (based in age)? Drink large amounts of water to decrease the amounts of vasopressin and cAMP in the body which is known to increase the size of kidneys.

How should the lifestyle plan change? Well since the kidneys are responsible for filtering water from the body, we recommend that the patient drink no sugar fluids such as soda in addition to staying from all forms of alcohol.

How does the lifestyle and health plan address specific genetic/physiological features? We would want to avoid all actions that would place stress on the kidneys. It would be our goal as physicians to keep both kidneys functioning as long as possible to keep the patient off of dialysis, which would be detrimental to their health.

What are the current medicines on the market to address disease? There are no current medicines on the market that directly treat polycystic kidney disease, but there are medications to treat the pain caused by PKD (aspirin, and Ibuprofen), and medication that treat high blood pressure (statins etc.). There are drugs in clinical trials for vasosuppression, but they are not yet approved.

What more is needed in medical research? Since there are no drugs approved for the treatment of PKD I would start there. Research could be conducted to identify a new drug that will help patients keep their kidneys functioning longer so that they will not have to go on dialysis, or even have their kidneys removed.

Lecture Material

Lecture- Central Dogma of Molecular Biology

The lecture is to introduce RNA transcription and protein translation. Students will learn the differences between DNA and RNA, the types of RNA, transcription, the genetic code, and polypeptide synthesis.

Lego Activity

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Printable instructions, student data sheet/pre-lab questions, and answer key can be found at: www.asbmb.org/912activity/

Purpose:

To understand that different cells build different proteins because they use different genes of the same DNA molecule.

Overview:

Students will work in small groups (4-5 students). Each group will take on the identity of a different cell type. They will use Lego “amino acids” to build a unique “polypeptide” chain.

Materials:

For each student:

- ☐ Photocopy of assignment backed with data sheet.

For each group:

- ☐ Copy of the protein “recipes”
- ☐ Copy of the Lego genetic code

On a shared table, the “cytoplasm” (since the blocks represent amino acids):

- ☐ 30 Green Lego Blocks
- ☐ 40 Yellow Lego Blocks
- ☐ 65 Red Lego Blocks
- ☐ 45 Blue Lego Blocks
- ☐ 40 White Lego Blocks
- ☐ 20 Black Lego Blocks

Posted at the front of the class, the “nucleus”:

- ☐ The DNA molecule which will be used by all groups

Procedure:

1. Pass out the assignment and data sheet.
2. Have the students answer the pre-lab questions (10 minutes)
3. Discuss the answers to the pre-lab questions (5 minutes)
4. Assign each group a cell type.
5. Students go to their groups and copy the recipe on their data sheet:
6. Now **ONE** person goes to DNA molecule and copies the nucleotides for the genes from the DNA molecule, one gene at a time:
7. Back at the lab station, the student reads off the DNA nucleotides while another student transcribes it into RNA codons:
8. The first person goes back to the DNA molecule to copy the next gene. The second person now uses the Lego Genetic Code to decode the RNA codons into Lego blocks:
9. The third person now goes to the table and gets the Lego blocks, **ONE** at a time, and brings them back to the lab station.
10. The second person now takes the block and adds it to the tower.
11. When all the work is done, and the tower is made, each student fills in his/her entire data sheet and colors the boxes on the data sheet, and answer the questions.

Lego “Genetic Code”

| RNA | Block |
|-----|--------|
| UGG | Blue |
| CGC | Yellow |
| UUA | Red |
| CUA | White |
| UGC | Black |
| CAA | Green |

Lego “Polypeptide” Recipes

| Cell Type | Genes |
|------------------|------------------------------|
| Liver Cell | 4, 2, 4, 2, 3, 3, 4, 4, 3, 3 |
| Nerve Cell | 5, 3, 5, 2, 5, 1, 1, 1, 1 |
| Muscle Cell | 3, 5, 1, 3, 5, 1, 3, 5, 1, 3 |
| Skin Cell | 1, 2, 2, 1, 3, 3, 5, 4 |
| Bone Cell | 1, 5, 3, 4, 1, 1 |
| Lung Cell | 3, 1, 3, 2, 4, 5, 2, 3, 1, 3 |
| Kidney Cell | 2, 5, 2, 4, 3, 2, 4, 2, 3 |
| White Blood Cell | 5, 4, 3, 1, 2, 3, 4, 2, 2 |

1

2

3

4

5

AATGATACC ACGGCGAAT GTTGATAAT GTTGCGAAT ACCGCGACC



Scientist Interview

1. Prepare a list of scientists students can either interview in person or via the phone.
2. Have students write cover letter asking scientist for interview. Use template provided below as a model.

Dear Dr. _____

My name is _____ and I am writing to express my interest and to learn more about your research involving _____. I am an 11th grade student at High Tech High North County and we are researching _____ to create lessons that may be disseminated to schools around the area. My hope is to better understand current research occurring that might effect the conservation of _____.

If possible, I would jump to the opportunity to ask a couple questions via email or interview about what led you to your current work and your personal perspectives about _____.

With permission, your guidance and work would be shared as part of a school project and in lessons that we create and share with elementary and middle school students. Please let me know if you have any questions and if you are able to talk or email back answers to quick questions.

Thank you so much for taking time out of your busy schedule.

Sincerely, _____

3. During interview, use following questions provided below as a starting point.

Personal (Student) Introduction if not yet given.

Interview Questions

1. Your name, position, organization/laboratory/hospital.
2. How did you come to research _____?
3. Can you tell me a little about your current work and its implications?
4. We are interested in what your life is like as a researcher/clinician on a day to day basis. Is there something that you would like to share with the general public or community that cares about prevention, therapies and cures for the disease?
5. As part of the 11th grade project, we are creating an art piece in studio art that I hope can serve to represent a piece of your work.
6. Is there an image or idea that represents what you do that I can work towards to represent the important things that you do? If you don't have ideas now, we will be starting the artwork on _____, and would love to hear any ideas before then. Anything would help and would be amazing!

Art Project

Based on scientist interview, students will create an artistic representation of the scientist's research. The art piece is to demonstrate the researcher's work, which means the student has to understand on a basic level the scientific and medical implications of the work. The art piece can be shared with the scientist, or kept on display in the classroom. Multiple "drafts" are encouraged to yield a high quality final product.

Examples of art projects from this activity can be found here:

<http://sleader.weebly.com/in-sickness-and-in-health.html>