Using Genomics to Understand Patterns of Inheritance
GENA Project Summary

Dr. Alexis Nagengast, Professor of Genetics, Weidner University
John Politano, Science Teacher, Garnet Valley High School

In November, Dr. Alexis Nagengast visited Garnet Valley High School to give a presentation on genomics and fruit fly variants. The students were taking Mr. Politano’s course called “Evolutionary Biology and the Environment”. The purpose of the lesson was to introduce future science professionals to how gene mutation, regulation, and expression is tied into the study of evolution. They also learned how to use the online databases to search for human genes, protein sequences, and those of other organisms using the BLAST feature. The goal was to understand why the databases are important and why it is beneficial to study to DNA of other simpler organisms to give us insight on the mechanisms of our own genetics and how we can use these concepts to potentially cure human disorders in the future.

On Day 1, Mr. Politano set the stage for Dr. Nagengast’s visit. He gave a brief survey to address students’ misconceptions regarding the ideas that “all mutations are bad.” and that there is a “one gene, one protein” relationship in a eukaryotic cell. They watched a video on the Human Genome Project by NOVA, took notes for a few minutes off of a Power Point presentation designed by Mr. Politano, and discussed the video, their misconceptions, and Dr. Nagengast’s visit the next day. The students were excited to see her fruit fly variants up close and to ask her questions about her very important work at Widener University.

On Day 2, Dr. Nagengast’s visit went very well. A preliminary question was posed to the students before they observed the flies: “WHY IS THERE VARIATION IN THE FRUIT FLY POPULATION THAT DR. NAGENGAST HAS BROUGHT ALONG WITH HER TODAY? HOW CAN WE USE THESE VARIANTS TO LEARN ABOUT OUR OWN GENETICS?” The students then spent 20 minutes looking at the flies through our classroom stereoscopes and asking questions about what they were observing. They were very intrigued to hear about her work after having observed her specimens.

Dr. Nagengast then spent some time explaining what these specimens are utilized for in the lab, how they are manipulated to achieve the desired variations, and the overall goals of her research. After Mr. Politano distributed the instructions and rubric for the performance assessment, she used an example, hemophilia, to demonstrate how to access and navigate through the NCBI online databases. She showed students how to run a search for the genetic evidence of the disorder, and how to find other known disorders on the same chromosome, in this case, the X chromosome. Mr. Politano has Internet access and an overhead projector in his classroom, so the multimedia demonstration was easy to perform. Students watched intently and took notes since they would have to repeat the same thing on their own workstations for their chosen disorder and chromosome.
Students then went into the adjacent computer lab for about 20 minutes and began their assignment. They were told that before the end of the period, their only goal was to find their chromosome using NCBI and OMIM, identify the gene map locus on the chromosome of the disorder they chose off the rubric, and find the actual genetic evidence which shows the gene and protein sequencing mismatches on the evidence viewer. A few students were a little confused, but the session went surprisingly well for the first time, as most students were able to reach their goal for the period. Those who did not returned to class the next day during our school’s 50 minute enhancement period to try it again, where they were able to get a little more individual attention from their instructor.

One week later, students performed their presentations. They had to construct a poster of their chromosome with the loci of four disorders, make a print-out of their genetic evidence with at least five genetic or protein mismatches circled, and write a 150-word summary of the research. The presentation went well as students confidently explained their work and fielded questions from their classmates. It seemed apparent that students learned the chromosomal positions of many known human genetic disorders and became aware of the actual biochemical mechanisms through which these disorders are expressed. They enjoyed the lesson, guest speaker presentation, the project, and especially the fruit flies.
Using Genomics to Understand Patterns of Inheritance

Dr. Alexis Nagengast, Professor of Genetics, Weidner University
John Politano, Science Teacher, Garnet Valley High School

Courses:
Evolutionary Biology and the Environment, Biology I Honors (modified version)

Misconceptions
- All mutations are bad.
- One gene, one protein.

State standards
- PA 3.3.10.C - Describe how genetic information is inherited and expressed.
  - Describe mutations effects on a trait’s expression.
  - Explain the relationship among DNA, genes, and chromosomes.
- PA 3.3.12.B – Analyze the chemical and structural basis of living organisms.
  - Describe potential impact of genome research on the biochemistry and physiology of life.
- PA 3.3.12.C - Explain gene inheritance and expression at the molecular level.
  - Analyze gene expression at the molecular level.
  - Describe genetic engineering techniques, applications, and impacts.

Big Ideas
- Genes are units of heredity in living things.
  - Genes are made up of DNA, which are made of nucleotides.
  - Mutations are changes in the DNA sequencing which could potentially lead to advantageous or disadvantageous traits in living things.
  - Not all genes are expressed in every cell in a multicellular organism.
  - We can use the field of genomics to analyze an organism’s nucleotide and protein sequencing and compare genetic variations among species.
- Evolution is driven by changes in the relative frequencies of heritable traits in a group of organisms over time.
  - Traits are inherited, passed through the generation through reproduction; reproduction is a driving force of evolutionary change.
  - Evolution can not happen without variation, two sources of which are mutations and gene shuffling.
  - All living things share certain genetic similarities also passed down over 3.5 billion years of evolutionary history.
  - Adaptations often persist in a population because they are advantageous.
  - Evolution results from selection acting upon variation within a population.

Students will be able to …
- Choose the correct database to analyze specific DNA sequences.
- Identify DNA sequences for specific alleles.
- Identify potential nucleotide and amino acid changes in certain genes.
• Analyze gene expression in various human tissues.
• Analyze nucleotide and protein variation in the same gene among species.
• Evaluate use of genetic information to trace evolutionary relationships.

Materials:
• Computer lab for exploration of NCBI DNA database
• Fruit fly variants
• Stereoscopes
• MS PowerPoint and classroom presentation materials
• Video: NOVA – Cracking the Code of Life

Skills students will use in this lesson:
• DNA analysis
• Use of the stereoscope
• Internet and computer skills
• Practical application of concepts previously learned in class

Prerequisite knowledge
• Principles of classical Mendelian genetics, DNA and chromosome structures, replication, protein synthesis, mutations, sources and importance of genetic variation, gene regulation, evidence of evolution, natural selection and genetic drift

Learning cycle (5 E’s Instructional Model)
• Engage
  o Addressing misconceptions: student preliminary survey.
  o Intro video and brief PowerPoint on the HGP.
• Explore
  o Discussing misconceptions on survey.
• Explore/Observe
  o Lab: Observation of Fruit Fly Variants from Dr. Nagengast’s lab.
• Explain
  o Guest speaker presentation: Dr. Alexis Nagengast of Widener University.
    ▪ Intro to genomics.
    ▪ Importance of fruit fly genome in genetics research.
    ▪ Mutations in fruit flies.
• Extend
  o Exploration of DNA databases using NCBI.
• Evaluate
  o Student project on using databases to understand genetic disorders.

Formative Assessment: Unit Project: DNA Databases. Students will be given one week to complete project and give classroom presentations.
Summative Assessment: Students will be given a pre and post lesson survey to address misconceptions about gene regulation and genomics. They will also be given a brief 10 minutes quiz on the databases, gene regulation, and the study of genomics.

**Lesson Plans – 80 minute periods**

**DAY 1**

After having just completed a textbook assignment on gene regulation, students have been given a quiz on the topic. They have already studied protein synthesis, gene activation, and chromosomal structure. Thirty minutes will be devoted to the end of this day to explain the Human Genome Project and explain the guest speaker presentation of Dr. Alexis Nagengast on Day Two.

Present preliminary inquiry questions: **WHY IS IT IMPORTANT TO STUDY THE DNA OF OTHER ORGANISMS, AS WELL AS HUMANS’ DNA? WHAT CAN WE LEARN ABOUT THE DNA OF FRUIT FLIES THAT MAY HELP US FIND CURES FOR HUMAN GENETIC DISORDERS?**

- Addressing misconceptions: student preliminary survey. (5 minutes)
  - Students will take a brief survey about what they learned about genes and proteins. Please refer to “Student Survey”.
- Intro video: NOVA – Cracking the Code of Life: “The Finish Line” (10 minutes)
- Power Point: HGP (10 minutes)
  - Followed by a brief discussion on the societal impact of the completion of the project and continued research on human DNA as well as other organisms’ such as a fruit fly. Please refer to “Lesson: HGP” for complete presentation on the topic.
- Discussing misconceptions on student survey.

**DAY 2**

On this day, students will take part in the guest speaker presentation, which will include a stereoscope lab observing Dr. Nagengast’s fruit fly variants, and an introduction in the online DNA databases.

- Lab: Observing Fruit Fly Variants (30 minutes)
  - Preliminary question: **WHY IS THERE VARIATION IN THE FRUIT FLY POPULATION THAT DR. NAGENGAST HAS BROUGHT ALONG WITH HER TODAY? HOW CAN WE USE THESE VARIANTS TO LEARN ABOUT OUR OWN GENETICS?**
  - Dr. Nagengast will bring variants form her lab, including eyeless and wingless fruit flies. Students observe and learn that manipulation of these specimens helps geneticists understand the mechanisms of protein synthesis and gene mutations.
• Dr. Nagengast presentation – discussion of her work at Widener University. (10 minutes)
  o Time for students’ questions.
• DNA Database Demonstration (20 minutes)
  o Students will be given the project assignment and Dr. Nagengast will go through a brief walk-through of the OMIM features on the classroom computer overhead projector using www.ncbi.nlm.nih.gov. We will use an example disease, hemophilia, to demonstrate how to through the site and obtain the disease and mutation information needed for the project. Please refer to “Unit Project: DNA Databases” for more details on student performance assessment.
• Multimedia Project: DNA Databases (20 minutes)
  o Students will then choose a human genetic disorder, and begin searching for their gene on www.ncbi.nlm.nih.gov using the computer lab adjacent to Mr. Politano’s classroom. Dr. Nagengast and Mr. Politano will circulate through the room answering questions as the students access the OMIM web application, find their gene, and try to identify an example of gene and protein mutations. Please refer to “How to Use the NCBI Database” worksheet for instructions.

DAY 3

After having given the students an additional week to put together their projects, students will present their findings to the class in a brief 5-minute lesson. They will discuss their disorder, 3 other disorders on the chromosome they have chosen or been assigned, and show the class an example on their print-out where the gene mutation results in a potentially negative protein mutation.
  • Post-Lesson Survey – same one as before. Compare and discuss answers to address student misconceptions. (10 minutes)
  • Gene Regulation Quiz (10 minutes)
  • Student Presentations (5 minutes each – 60 minutes total)
Student Survey: Addressing Misconceptions about
The Human Genome Project

1. All mutations are bad.
   AGREE    DISAGREE    DON’T KNOW

2. One gene can only make one protein in a cell.
   AGREE    DISAGREE    DON’T KNOW

3. The Human Genome Project has been completed.
   AGREE    DISAGREE    DON’T KNOW

4. It is only important to understand and study human DNA in order to
   find cures for human diseases.
   AGREE    DISAGREE    DON’T KNOW
HGP

• In 1990, the United States led an effort to sequence the entire human genome - all 3 billion letters and 30,000 genes.
• The HGP was completed in 2000.
• Why is it important to do this from a biomedical perspective?
The “parts list” is essential in order to find cures.

Video:
NOVA – Cracking the Code of Life: The HGP
Ethical Considerations

• Would you want to know if you were more likely to develop a disease if there was no cure?
  – BRCA gene.

• What would happen to our society if we were allowed to design our offspring’s bodies?
  – Gataca
How to use NCBI to search for DNA and protein sequences:


2. Type in disease name in the search bar at the top, select “OMIM” database to the left, and click “go”.

3. Search the description for the following information:
   a. Which gene when mutated results in the disease.
   b. Which chromosome the gene is on.
   c. If the disease allele is dominant or recessive.

4. Click on the gene map locus for the desired gene.

5. On the next screen, there is a gray table. Again click on the gene location.

6. Scroll down to see the desired gene highlighted in pink or purple. You may have to click on the tiny blue arrow at the bottom of the chromosome segment to find your gene or may need to zoom out to get a bigger view of your chromosome. Once you find the pink or purple highlight gene ion the far left of the chromosome map, right-click it.

7. A small yellow window will appear. Click on “ev” to look at the genetic evidence for your gene.

8. Search for and circle 5 genetic mutations and explain in your essay.
Unit Project
NCBI Databases

Genomics is the study of an organism’s entire genome. Genomics includes efforts to determine the entire DNA sequence of organisms and fine-scale genetic mapping efforts. We can search genetic databases to explore nucleotide and protein differences and similarities in individuals within and among species.

For the genetic disorder of your choice, do the following:
1. Use the Internet to research information about the disorder including symptoms, incidence, treatment, and social issues.
2. Create a poster to present to the class about the disorder. The presentation should be about 5 minutes in length.
3. Use NCBI to investigate genetic mutations in the human population that contribute to the development of the disorder. Refer to the instructions “How to Use NCBI databases”.
4. Write a 150-word essay summarizing your research.
5. Print out all work and submit with your paper.

Choose a single-gene disorder from the list below.

- Cystic fibrosis (#219700)
- Hemophilia A
- Achondroplasia
- Huntington’s Disease
- Duchenne Muscular Dystrophy
- Sickle Cell Anemia
- Marfan’s Syndrome
- PKU
- Colorblindness
- Citrullinemia
- Fabry Disease
- Osteogenesis Imperfecta
- Breast Cancer
- Retinoblastoma
- Tay-Sachs Disease
- Albinism
- Gardner Syndrome
- Factor 5 Deficiency
## Unit Project Rubric

### Family Pedigree Chart

<table>
<thead>
<tr>
<th>Activity</th>
<th>10</th>
<th>5</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focus during project; time on task</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Preliminary disease presentation and poster</td>
<td>20</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Nucleotide and protein sequence print-out</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Identification of Open Reading Frame</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Identification of nucleotide and amino acid mutations</td>
<td>20</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Written summary</td>
<td>20</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Internet research of disease, including works cited</td>
<td>10</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>