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Learning – Pseudogenes and Using Python to Compare Gene Mutations in Humans and Other Organisms

1. **Lesson Overview** Students will be able to use and modify a Python Code to determine the differences in genes across evolutionary time.

Lesson is to be completed over a period of 3 days (or three 50-min classes)

2. **Focus Question/Big Idea/Learning Goal and Learning Outcomes/Objectives**

Learning Outcomes/Objectives

- What is a pseudogene?
- What do pseudogenes tell us about common ancestry?
- What do pseudogenes tell us about natural selection?
- What are different types of mutations and how do they occur?
- How do mutations impact organisms?

3. **Standards Table: Drawn from PADE Biology Keystone Exam Assessment Anchors and Eligible Content Content**

Anchor Descriptor	BIO.B.1.2 Explain how genetic information is inherited. BIO.B.2.1 Compare Mendelian and non-Mendelian patterns of inheritance. BIO.B.3.1 Explain the mechanisms of evolution. BIO.B.3.2 Analyze the sources of evidence for biological evolution.
Eligible Content	BIO.B.1.2.2 Explain the functional relationships between DNA, genes, alleles, and chromosomes and their roles in inheritance. BIO.B.2.1.2 Describe processes that can alter composition or number of chromosomes. BIO.B.3.1.2 Describe the factors that contribute to the development of new species. BIO.B.3.1.3 Describe how genetic mutations may result in genotypic and phenotypic variations within a population. BIO.B.3.2.1 Interpret evidence supporting the theory of evolution.

4. Academic Language Demands/ Vocabulary/Symbols

1. **Pseudogene**- a section of a chromosome that is non-functional and an imperfect copy of a functional gene.
2. **Gene**- segment of DNA that codes for a particular protein
3. **Genome**- all the genes in an individual or a species
4. **Mutation**- A random change in the nucleotide sequence of the genome that can be passed on to daughter cells.
5. **Common Ancestor**- of any set of organisms is the most recent individual from which all organisms in a group are directly descended.
6. **Natural Selection**- organisms with more advantageous traits for their environment survive and reproduce more often (This causes traits in the population to change over time).

5. Prior learning and prerequisite skills

Students should have covered the topics of genetics and evolution before starting this lesson.

6. Materials:

- Computers (one per student is preferred, but one per group of 4 students is possible)
- Internet access
- Access to the following websites:
 - <https://www.ncbi.nlm.nih.gov/genbank/>
 - <https://blast.ncbi.nlm.nih.gov/Blast.cgi>
 - <http://www.ebi.ac.uk/Tools/msa/muscle/>
 - <https://genome.ucsc.edu/>
 - <http://www.ensembl.org/index.html>
- Google Slide document (see attached)
- Paper/pencil for students
- Student Packet (1/student)

7. Safety concerns and disposal N/A

8. Learning and Teaching Experiences – Engage, Explore, Explain, Elaborate, Evaluate

Time	
Engage	
20 Min.	<p>Warm-Up: Create a Venn-Diagram in groups of 4 comparing/contrasting the characteristics of Humans and another mammal of your choice. Review student responses.</p> <p>Follow-up Questions:</p> <ol style="list-style-type: none"> 1. What makes these organisms have these characteristics? Answer: Genes, Natural Selection 2. Why were some of these characteristics able to stay the same in two different organisms? Answer: Important for Survival 3. What happened to the genes that are no longer seen in humans? Answer: They became mutated (lead this into the idea of non-functioning genes aka pseudogenes) <p>Define Pseudogene- a section of a chromosome that is non-functional and an imperfect copy of a functional gene. break apart term <i>pseudo</i>- imitating/fake <i>gene</i>- set of DNA that codes for a particular trait</p>
Explore	
30 min.	<p>Assign each group one of the following pseudogenes: (https://en.wikipedia.org/wiki/List_of_disabled_human_pseudogenes for quick reference) WNT3A, NCF1C, GULOP, IRGM, hHaA, DEFT1P, urate oxidase pseudogene, photolyase pseudogene</p> <p>Students will use https://www.ncbi.nlm.nih.gov/genbank/ to research their assigned pseudogene. <i>It may be helpful to demonstrate how to research gene on this website</i> Search→ click one search return → (to the right under “Analyze this Sequence”) Run BLAST → (Scroll to bottom of page) BLAST (blue button)</p> <p>For additional information on pseudogenes in general, go to http://www.darwinwasright.org/pseudogenes.html .</p>

	<div>See accompanying function.</div> <table> <tr> <th>Pseudogene</th><th>Function</th></tr> <tr> <td>WNT3A</td><td>associated with the growth of a tail (and general development)</td></tr> <tr> <td>NCF1C</td><td>associated with a type of white blood cell</td></tr> <tr> <td>GULO/GULOP</td><td>associated with the production of Vitamin C</td></tr> <tr> <td>IRGM</td><td>associated with the immune system</td></tr> <tr> <td>hHaA</td><td>associated with fur-like body hair</td></tr> <tr> <td>DEFT1P</td><td>associated with the immune system</td></tr> <tr> <td>urate oxidase pseudogene</td><td>associated with the processing of uric acid (important in meat digestion)</td></tr> <tr> <td>photolyase pseudogene</td><td>associated with repairing DNA damaged by UV radiation</td></tr> </table>	Pseudogene	Function	WNT3A	associated with the growth of a tail (and general development)	NCF1C	associated with a type of white blood cell	GULO/GULOP	associated with the production of Vitamin C	IRGM	associated with the immune system	hHaA	associated with fur-like body hair	DEFT1P	associated with the immune system	urate oxidase pseudogene	associated with the processing of uric acid (important in meat digestion)	photolyase pseudogene	associated with repairing DNA damaged by UV radiation
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Explain																			
25 min.	<p>Have groups explain to the class the original function of their pseudogene. Emphasize that students should try to explain the function in their own words.</p> <p>Ask students why they think that humans are able to survive without the use of these genes.</p> <ul style="list-style-type: none"> Answer: Some code for things we do not need anymore (tail, body hair), some code for something that are not so significant that we could not survive (less efficient at digesting meat) <p>Have students generate a list of other things that they think might be pseudogenes.</p> <ul style="list-style-type: none"> Answers will likely include things that humans do not have anymore 																		

Elaborate	
25 min.	<ol style="list-style-type: none"> 1. Have students look up their assigned gene in GenBank (https://www.ncbi.nlm.nih.gov/genbank/). 2. Students should click the link for their gene. 3. Under “Analyze this sequence”, click “Run BLAST”. Alternatively, copy the ascension number of the gene and visit the BLAST website (https://blast.ncbi.nlm.nih.gov/Blast.cgi) 4. Check the box for your gene (the first option). Check the box for an unrelated organisms (scroll down to an organism with a non-human scientific name). 5. Click Download→ FASTA(Aligned Sequence). 6. Go to http://www.ebi.ac.uk/Tools/msa/muscle/ 7. Copy the contents of the file that you generated in BLAST into the box. 8. Change the output format to Pearson/FASTA. 9. Hit “Submit”. 10. Hit “Download Alignment File” 11. Right Click → Save As → “gene_name.fasta”. For example, WNT3A would be wnt3a.fasta 12. Save the file to the desktop 13. Run pseudogene.py
Evaluate	
30 min	<p>Students will complete a written report in which they perform a visual survey of the two aligned genomes and analyze the results of pseudogene.py. Students will answer additional questions regarding mutations and their relation to natural selection.</p> <ul style="list-style-type: none"> • Students should include a screenshot of results after running the program in Python. • Conclusion Questions: <ul style="list-style-type: none"> ○ What types of mutations did you see between the human pseudogene and the functioning gene? Do you think that these types of mutations always have a large impact? ○ Do you think that non-functioning genes have more or fewer mutations than a functioning gene? Support your answer. ○ Why do biologists study pseudogenes? ○ Why do biologists use computers to study genomes?
Extension	
	<p>Dissect the bits of code in in the python program to explain what each statement means and its placement in the code.</p> <p>Students will construct a POE chart (see below)</p>

PREDICT (P)	OBSERVE (O)	EXPLAIN (E)
<p>predict what the code means*</p> <p><i>Students will write down their predictions, discuss as a class.</i></p> <p>*you may want to start out with a specific section of the program code</p> <p>Have students work in groups to modify code to to perform a different function.</p>	<p>Run the code...What happened?</p> <p><i>Students will write what happened when the program ran.</i></p>	<p>Why did this happen?</p> <p><i>This is a good opportunity to discuss the syntax of coding and what each thing means.</i></p>

9. Real World Connections explored within the lesson

- Students will be studying and aligning real genes in real organisms.
- Students will be using methods similar to those used by real geneticists.
- Students will be analyzing real data.

10. Differentiation and other modifications

- Research methods, genome browsing, and running of python program will all be modeled by teacher.
- Pair stronger students with weaker students

- Provide information on each of the pseudogenes for the groups to read

11. Homework *(optional)*

Students will write a paragraph about a pseudogene that was presented by another peer group.

If students are using their own laptops, it may be useful to ask them to download Python and IDLE on their laptops for homework.

12. References and Acknowledgements

NCBI GenBank

NCBI BLAST

EBI MUSCLE

Temple University

Dr. Jody Hey

Dr. Arun Sethuraman

Dr. Andrew Webb

13. Supplementary Materials

- Student Packet containing:
 - Chart of pseudogenes
 - Vocabulary list with blank definitions
 - Instructions for downloading gene files
 - Instructions for opening and running IDLE on chosen computer system
 - Analysis Questions
- Google Slide (see attached)