

PSEUDOGENE SUITE  
Lesson A: WHY DO WE NEED VITAMIN C IN OUR DIET?  
or...Why do we carry old inactive genes in our genome?  
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adapted for ENSIweb by L. Flammer

**SYNOPSIS:**

Students compare the DNA sequence data for a portion of the rat GULO gene (which helps make vitamin C) to the corresponding sequence in the inactive human GULO gene by translating the sequences and by aligning them. This lays ground work for exploring pseudogenes and the significance of these DNA sequences in recognizing shared common ancestry vs the notion of "intelligent design" (Lesson B).

**MAIN CONCEPT:**

Mutation may create an inactive version of a gene (an inactive allele), and, over generations, the active gene (allele) may be lost from the species, leaving only the inactive gene (allele).

**ASSOCIATED CONCEPTS:**

1. Unlike most mammals, humans cannot synthesize Vitamin C and must ingest it.
2. Remnants of once functional genes can be found in the abandoned "junk" segments of an organism's DNA.
3. A single-base deletion in a DNA coding sequence shifts the reading frame.
4. A frameshift mutation may lead to premature chain termination by creating a stop codon.
5. A frameshift mutation may alter the sequence of amino acids from that point on in the chain.
6. Enzyme function is likely to be lost if the protein chain is greatly shortened or its amino acid sequence is dramatically changed.

**ASSESSIBLE OBJECTIVES:**

1. Predict the likely effects of a frameshift mutation on the amino acid sequence of an enzyme and on enzyme function.
2. Propose a scenario to explain the occurrence in one species of an inactive DNA sequence similar to that of an active gene in another species.

**MATERIALS**

Student Handouts (3 sheets: Background, Worksheet and Genetic Code Chart)  
Key to Worksheet (for teacher)

**TIME:**

45 minutes

**TEACHING STRATEGY:**

Excellent Teacher Background on Pseudogenes and Intergenic Analyses can be found online at:

<http://bioinfo.mbb.yale.edu/genome/pseudogene/>

1. This lesson assumes a basic understanding of enzyme structure/function and of gene expression (protein synthesis). It is intended to be the first lesson (A) in this suite of three lessons, to be followed by Lesson B: "What Can Pseudogenes Tell Us About Common Ancestry?"
2. This lesson would fit nicely near the end of an introductory unit on DNA structure and function., or, in concert with the other two lessons in this suite, it would be appropriate in a unit on evolution, or classification and biological relationships.
3. Prepare enough copies of the Student Handout (not stapled) for every student or pair of students.

**PROCEDURES:**

Students may work alone, or preferably in pairs.

1. Either present the background information on scurvy and vitamin C, or pass out the Student Handout and have students read the Background information.
2. Explain to students that comparing the entire sequences for the functional rat GULO gene and the inactive human GULO gene is not practical in our time frame, so they will compare only a sample portion of the two sequences.
3. Students use a Genetic Code Chart to translate the partial rat sequence and the corresponding human sequence given in the Worksheet. You might need to demonstrate this process.

4. Students compare the resulting sequences and then examine the alignment to determine how specific differences in the DNA sequences relate to differences in the amino acid sequences.
5. Students apply their observations to propose a biologically reasonable explanation for the presence of the inactive GULO gene in humans. (Note that the term "pseudogene" is not used in this activity, but is introduced in the companion lesson B: "What Can Pseudogenes Tell Us About Common Ancestry?")

## DISCUSSION

6. Lead a discussion in which teams share their answers to the questions in the Student Handout. (Refer to the Answer Key.)
7. Note: Students may have the misconception that any nonfunctional alleles that occur due to mutation should, over generations, be somehow "removed" by Natural Selection. If this point should come up, remind students that for Natural Selection to be able to select against a nonfunctional allele, the individuals in the population carrying the nonfunctional allele would have to be less likely to survive and reproduce as a result. If vitamin C were readily available in food, the inability to make it would be of no consequence. Under these circumstances, there could be no Natural Selection and the frequency of the nonfunctional allele could increase over generations by chance, such that eventually the functional allele could be lost completely from the species. (Although one could argue that having useless DNA imposes a metabolic burden, such a difference for just one gene is expected to be extremely slight.)

Even if they understand that the active (functional) allele could, over generations, be lost from the species by chance, students may expect the remaining nonfunctional allele (now appropriately called a pseudogene) to be somehow removed by Natural Selection. Remind them that, for Natural Selection to occur, there must be at least 2 different genotypes present. Point out that if ALL individuals carry only the pseudogene, then Natural Selection cannot occur. Thus, once a nonfunctional allele by chance becomes the only surviving allele for that gene in the species, it is likely to persist indefinitely. (If at some future time individuals are born that happen to lack the gene entirely, THEN the pseudogene might be eventually lost by chance or removed by Natural Selection.)

## ASSESSMENT & EVALUATION:

1. Check student worksheets to determine whether they were able to translate the sequences correctly.
2. Ask students to explain why a frameshift mutation is more likely than a single-base substitution to dramatically affect enzyme activity.
3. Ask students to give a biologically reasonable explanation for why humans have an inactive GULO gene.

## EXTENSIONS & VARIATIONS:

1. This activity was meant to be used as an introduction for lesson B: "What Can Pseudogenes Tell Us About Common Ancestry?"
2. The data from which these partial sequences were taken consists of the complete coding sequence corresponding to rat exon 10 from the rat, human, chimpanzee, orangutan, and crab-eating macaque. This data is available through Biology Workbench for computer manipulation. See the Biology Workbench GULO Activity (Lesson C in this suite).
3. Humans lack the enzyme "uricase" but have an inactive DNA sequence similar to that of the functional uricase gene. The functional baboon protein consists of a chain of 304 amino acids. In the corresponding human DNA sequence, codon 33 is TGA, instead of CGA. Have students use the Genetic Code chart to predict how such a difference would affect enzyme structure and activity.

## REFERENCES:

- Nishikimi, M.; Fukuyama, R.; Minoshima, S.; Shimizu, N.; Yagi, K.:  
Cloning and chromosomal mapping of the human nonfunctional gene for L-gulono-gamma-lactone oxidase, the enzyme for L-ascorbic acid biosynthesis missing in man.  
J. Biol. Chem. 269: 13685-13688, 1994. PubMed ID : 8175804
- Nishikimi, M; Kawai, T; Yagi, K.:  
Guinea pigs possess a highly mutated gene for L-gulono-gamma-lactone oxidase, the key enzyme for L-ascorbic acid biosynthesis missing in this species.  
J Biol Chem 267:21967-72, 1992. PubMed ID: 1400507

Excellent Resource for clear Background Information: Pseudogenes & Intergenic Analyses (Yale):  
<http://bioinfo.mbb.yale.edu/genome/pseudogene/>

#### ATTRIBUTIONS:

1. Original Source: This activity was developed by Prof. Mary Ball and Steve Karr of Carson-Newman College for use in a high school biology course or a college-level introductory biology course. References used as a source of information, ideas, and sequences are listed on the References page. (The actual articles were not consulted. The abstracts and data were accessed through PubMed.)

2. Edited / Revised for website by L. Flammer 2/2002; again 7/2003