

GENE SUITE: Lesson A: Why do we need Vitamin C in our diet?

BACKGROUND

Scurvy and the Discovery of Vitamin C

In 1535, the Frenchman James Cartier sailed up the St. Lawrence River to Quebec City, Canada. Many of his sailors were suffering from “scurvy”, a disease that was common aboard ships that had been at sea for several weeks. Sufferers of scurvy experienced bleeding gums, bruising, and eventual death. The Iroquois Indians suggested a remedy made by boiling the leaves and bark of a native tree to make a sour “tea”. The remedy worked, but scurvy continued to plague sailors for the next 200 years.

By the early 1700’s, the association between scurvy and diet was well known, but it was unclear whether only certain sour substances worked. In 1747, the British physician James Lind did a study using 12 sailors suffering from scurvy. In addition to their normal shipboard diet, each received one of the following dietary supplements: 2 oranges and 1 lemon, vinegar (acetic acid), sea water, sulfuric acid, apple cider, or a mixture of drugs. Within a week, the two who ate 2 oranges and 1 lemon each day showed dramatic improvement. Lind later developed a method for concentrating and preserving citrus fruit juices and in 1795 the British Navy decreed that sailors receive a daily ration of lemon juice or lime juice. To this day, British sailors are referred to as “Limeys”.

The name Vitamin C was coined in 1913, but it wasn’t until around 1930 that its chemical structure was determined. Animal studies soon indicated that most mammals do not develop scurvy, even when there is no Vitamin C in their diet. Further research showed that most mammals actually synthesize Vitamin C and that the synthesis involves a series of enzymes, each coded by a specific gene. It was initially assumed that humans must ingest Vitamin C because we lack these genes.

In 1976 it was confirmed that humans lack the last enzyme in the series of steps needed to make Vitamin C. Imagine the surprise when, in 1988, researchers found evidence of a human DNA sequence very similar to that of the DNA sequence of the rat gene coding for the missing enzyme! In 1994, the human gene sequence, named GULO for the enzyme L-gulonolactone oxidase, was actually determined and compared to the rat GULO gene sequence, revealing a high degree of overall similarity but a number of significant differences.

Why can’t we produce the GULO enzyme?

Perhaps if we were to compare the human gene sequence to the rat GULO gene sequence, we would be able to identify possible reasons why human cells do not produce the GULO enzyme. Because the rat GULO gene is a very long DNA sequence, coding for a chain of 440 amino acids and containing several noncoding sequences, a complete comparison would be time-consuming.

PROCEDURE: We will look at just a part of the gene, the section coding for amino acids number 337 through 353, and the corresponding sequence in the inactive human GULO gene. On your worksheet “A” is the partial sequence from the rat GULO gene. Gene sequences are entered into sequence databases in such a way that, to translate the sequence using the Genetic Code Chart, work from left to right and look up each 3-letter codon in the chart. Place the corresponding amino acid (AA) in the space below its codon. (If you come to a TAA, TAG, or TGA, just stop translating.)

Name _____

Date _____

WORKSHEET A: Why Do We Need Vitamin C In Our Diet?

1. Translate this sequence from the rat GULO gene into its corresponding amino acid sequence:

AA#: 337 340 345 350 353

DNA: TAC/CCC/GTA/GAG/GTG/CGC/TTC/ACC/CGA/GGC/GAT/GAC/ATT/CTG/CTG/AGC/CCC

AA: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

2. Below is the corresponding sequence from the inactive human GULO gene. Translate this sequence:

DNA: TAC/CTG/GTG/GGG/GTA/CGC/TTC/ACC/TGG/AGG/ATG/ACA/TCC/TAC/TGA/GCC/CC

AA: _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

3. Circle each amino acid formed from the human GULO DNA sequence (above) which is same as the amino acid formed by the corresponding DNA in the rat GULO gene. How many match? How do the amino acid sequences compare? (Be specific.)

4. To see how differences in the gene sequences are related to the differences in the amino acid sequences, let's look at the two DNA sequences together, matching them letter for letter as best we can. This is called an "alignment" (see below). Mark with a small line each nucleotide in the human GULO sequence which differs from the corresponding rat GULO nucleotide. Count these.

TACCCCGTAGAGGTGCGCTTCACCCGAGGCGATGACATTCTGCTGAGCCCC (from Rat GULO gene)

TACCTGGTGGGGGTACGCTTCACCTGGAG-GATGACATCCTACTGAGCCCC (from Human GULO sequence)

5. How are the differences in the DNA sequences related to the differences in the amino acid sequences coded by this DNA segment? (Be specific.)

6. Based on the observed differences between the rat gene and the human gene, propose a general scenario whereby a mutation could create a nonfunctional version of a gene.

7. Applying your knowledge of the relationship between Vitamin C and diet, propose a scenario whereby a mutation in a functional GULO gene could create a nonfunctional version of the sequence and the functional gene could, over generations, be lost.