A Content Secondary Science Newsletter from the Southern Nevada Regional Professional Development Program

Science Dissected

Genetic Mutations
Model-Evidence Link Diagram (MEL)

Genetic mutations occur within organisms both during meiosis and mitosis. Students are often under the misconception that mutations are always harmful. This instructional resource is designed to introduce the concept to 6th grade students, providing them with evidence that will allow them to critically evaluate the two competing models regarding the effects of genetic mutation.

Model A: ***Genetic mutations almost always cause harmful change to an organism.***

Model B: ***Genetic mutations often cause no change to an organism. When mutations do cause change the change can be helpful or harmful to the organism.***

Evidence #1: The majority of mutations that happen during DNA replication are fixed by DNA repair proteins within the cell before the effect of the mutation is seen.

Evidence #2: Most mutations affect only parts of the DNA that do not contain instructions for a gene .

Evidence #3: Most mutations are silent or neutral; those that do make a change are mostly harmful with a small percentage simply making a change in function or providing an advantage.

Evidence #4: Whether a mutation is helpful, harmful, or neutral to an organism depends on the situation or environment at that time.

Evidence #5: All humans have hundreds of potentially harmful mutations that they have acquired.

The following is a suggestion for using this MEL with students:

1. Hand out the Genetic Mutations Model Evidence Link Diagram (page 1). Instruct students to read the directions, descriptions of Model A and Model B, and the four evidence texts presented.
2. Handout the four evidence text pages (pages 3-7).
3. Instruct students to carefully review the Evidence #1 text page (page 3), then construct two lines from Evidence #1; one to Model A and one to Model B. Remind students that the shape of the arrow they draw indicates their plausibility judgment (potential truthfulness) connection to the model.
4. Repeat for Evidence #2-5 (pages 4-7).
5. Handout page 2 for the students to critically evaluate their links and construct understanding.

Once students have completed page 2, they can then engage in collaborative argumentation as they compare their links and explanations with that of their peers. Students should be given the opportunity to revise the link weighting during the collaborative argumentation exercise. If time permits, have students reflect on their understanding of genetic mutations and create questions that they might explore in the future.

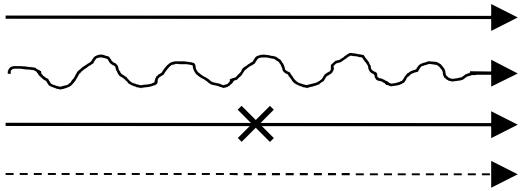
Archived Issues of Science Dissected, *http://www.rpdp.net/link.news.php?type=sciencedis*. ***Instructional Resource resulting from Plausibility, It's All About Connecting the Models Workshop co-sponsored by CPDD and SNRPDP Science March 6, 2012***

Written by: Charlotte Chambers

Name:_____ _____ **Period:**_____

Directions: draw two arrows from each evidence box. One to each model. You will draw a total of 10 arrows.

Key:



The evidence **supports** the model

The evidence **STRONGLY supports** the model

The evidence **contradicts** the model (shows its wrong)

The evidence has **nothing to do with** the model

Standard: L.8.A.2

Evidence #1
The majority of mutations that happen during DNA replication are fixed by DNA repair proteins within the cell before the effect of the mutation is seen.

Evidence #2
Most mutations affect only parts of the DNA that do not contain instructions for a gene.

Model A
Genetic mutations almost always cause harmful changes to an organism.

Model B
Genetic mutations often cause no change to an organism. When mutations do cause change the change can be helpful or harmful to the organism.

Evidence #3
Most mutations are silent or neutral; those that do make a change are mostly harmful with a small percentage simply making a change in function or providing an advantage.

Evidence #4
Whether a mutation is helpful, harmful, or neutral to an organism depends on the situation or environment at that time.

Evidence #5
All humans have hundreds of potentially harmful mutations that they have acquired.

Provide a reason for three of the arrows you have drawn. **Write your reasons for the three most interesting or important arrows.**

A. Write the number of the evidence you are writing about.
B. Circle the appropriate descriptor (**strongly supports | supports | contradicts | has nothing to do with**).
C. Write the letter of the model you are writing about.
D. Then write your reason.

1. Evidence # ____ strongly supports | supports | contradicts | has nothing to do with Model _____ because:

2. Evidence # ____ strongly supports | supports | contradicts | has nothing to do with Model _____ because:

3. Evidence # ____ strongly supports | supports | contradicts | has nothing to do with Model _____ because:

4. Circle the plausibility of each model. [Make two circles. One for each model.]

	Greatly implausible (or even impossible)									Highly Plausible
Model A	1	2	3	4	5	6	7	8	9	10
Model B	1	2	3	4	5	6	7	8	9	10

5. Circle the model which you think is correct. [Only circle one choice below.]

Very certain that Model A is correct	Somewhat certain that Model A is correct	Uncertain if Model A or B is correct	Somewhat certain that Model B is correct	Very certain that Model B is correct

Evidence #1: The majority of mutations that happen during DNA replication are fixed by DNA repair proteins within the cell before the effect of the mutation is seen.

WHAT CAUSES DNA MUTATIONS?

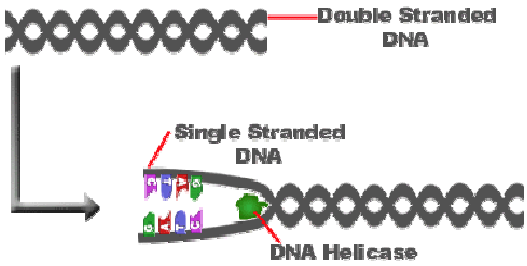
Mutations in DNA sequences generally occur through one of two processes:

1. DNA damage from environmental agents such as ultraviolet light (sunshine), nuclear radiation or certain chemicals
2. Mistakes that occur when a cell copies its DNA in preparation for cell division.

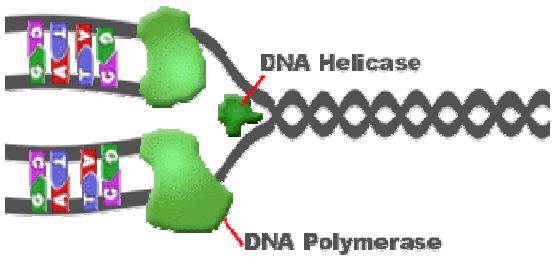
The following refers to mistakes created during DNA duplication

Prior to cell division, each cell must duplicate its entire DNA sequence. This process is called DNA replication.

DNA replication begins when a protein called DNA helicase separates the DNA molecule into two strands.



Next, a protein called DNA polymerase copies each strand of DNA to create two double-stranded DNA molecules.



Mutations result when the DNA polymerase makes a mistake, which happens about once every 100,000,000 bases.

Actually, the number of mistakes that remain incorporated into the DNA is even lower than this because cells contain special DNA repair proteins that fix many of the mistakes in the DNA that are caused by mutagens. The repair proteins see which nucleotides are paired incorrectly, and then change the wrong base to the right one.

Genetic Science Learning Center. "What Causes DNA Mutations?." Learn.Genetics 2 March 2012 http://learn.genetics.utah.edu/archive/sloozeworm/mutationbg.html

Evidence #2: Most mutations affect only parts of the DNA that do not contain instructions for a gene.

Why So Many Errors in Our DNA: 30 New Mutations per Lifetime

As scientists learn to read the instructions in our genes, they are discovering that much of our DNA is riddled with errors.

Fortunately, most of these errors are harmless. Considering the difficulties involved—the 6 feet of DNA in a human cell consists of 6 billion subunits, or base pairs, coiled and tightly packed into 23 pairs of chromosomes, all of which must be duplicated every time a cell divides—our general state of health is something of a miracle.

We each inherit hundreds of genetic mutations from our parents, as they did from their forebears. In addition, the DNA in our own cells undergoes an estimated 30 new mutations during our lifetime, either through mistakes during DNA copying or cell division or, more often, because of damage from the environment.

Bits of our DNA may be deleted, inserted, broken, or substituted. Most mutations affect only the parts of DNA that do not contain instructions for making a gene, so we need not worry about them. Problems arise only when an error in DNA alters a message that tells certain cells to manufacture a certain protein. Such messages are spelled out in varying sequences of the four chemical bases that make up DNA: adenine (A), thymine (T), guanine (G), and cytosine (C).

To stay alive and functioning, the human body requires a daily crop of billions of fresh protein molecules—about 40,000 different kinds of proteins that must be supplied in the right quantities, at the right times, and in the right places. We need hemoglobin to carry oxygen through the bloodstream, antibodies to fight foreign substances, hormones to deal with stress, neurotransmitters to evoke movements, emotions, and thought, and many other proteins to give structure to organs or speed up chemical reactions.

Much of the recent progress in reading DNA has come from analyses of genetic errors.

— Maya Pines

Howard Hughes Medical Institute. "Why So Many Errors in Our DNA:30 New Mutations per Lifetime". 2 March 2012

<http://www.hhmi.org/genetictrail/d100.html>

Evidence #3: Most mutations are silent or neutral; those that do make a change are mostly harmful with a small percentage simply making a change in function or providing an advantage.

About Mutation

A mutation is a permanent change in a gene (or more precisely in the DNA of the gene). We know a lot more about these now than they did back in the 1920s. This shouldn't surprise anyone.

The early geneticists thought all mutations were harmful. They studied these "errors" in genes in the hope that they would help them understand the way genes normally work. Remember that they had no knowledge of what genes were made of, or how they worked chemically. It turns out that they were wrong. Most mutations are silent (cause no real change) or neutral (cause a change that doesn't make any real difference); of those that do make a difference, most are harmful (at least in the organism's current circumstances), but a small percentage simply cause an alteration in function, or may even provide an advantage. Also, whether a mutation is harmful or not is sometimes situational — a change which is harmful in some situations may actually be beneficial in others.

We now know that genes are made of DNA, a magnificently simple/complex molecule which actually encodes a language. It carries information just as a book does. The language has 4 letters which form 64 three letter words.

The actual job that a gene does is to tell a cell how to build a particular protein. Thus, there is a gene with the instructions for making the protein insulin, and another for making the protein myoglobin, etc. Some proteins require more than one gene — for instance, hemoglobin, which requires at least two different genes plus some others to do associated building tasks. It's wonderfully complicated and marvelous.

Lynn Fancher, Associate Professor of Biology at the College of DuPage in Glen Ellyn, IL. “About Mutation”. 5 March 2012 <http://www.cod.edu/people/faculty/fancher/Mutation.htm>

Evidence #4: Whether a mutation is helpful, harmful, or neutral to an organism depends on the situation or environment at that time.

The question of whether a mutation is good or bad isn't as simple as it sounds. Yes, many mutations are devastating, but some are actually helpful. A mutation that broadens a parasite's host range is certainly helpful for the parasite — though I doubt the new host would agree. Mutations which create diversity can also be helpful. For instance, a mutation which slightly increases the size and robustness of a bird's beak may allow the bird to expand its potential food sources.

Then there's the question of circumstance. Whether a mutation is harmful, neutral or helpful can be very situational. An example from human evolution illustrates this very clearly.

The evidence clearly indicates that our ancestors came originally from Africa. All *Australopithecus* species were entirely confined to Africa, as was *Homo habilis*. In most of Africa sunlight, which contains potentially harmful ultraviolet radiation, is very direct and intense. UV causes sunburn, but it also causes skin cancer. Our skin pigmentation (melanin) absorbs UV. Thus, human ancestors living outdoors in Africa evolved to have very dark skin — lots of melanin to absorb enough UV to prevent them from getting skin cancer. Selective pressure in a situation like this strongly favors dark skin and makes any mutation for lighter colored skin harmful, since it reduces UV protection. So in this situation, mutations which decrease the amount of pigmentation in the skin are harmful. (Note: skin color in humans is a relatively complex trait genetically, involving several genes working together to determine the range of melanin the individual can make.)

However, eventually our ancestors meandered into other parts of the globe. When *Homo erectus* moved into Europe and Asia, the environmental conditions were quite different from those in Africa. In these temperate regions, sunlight was less intense, thus decreasing the selective pressure favoring dark skin, and allowing mutations for lighter skin color to become fixed in the population (in other words, increasing the diversity of skin pigmentation genes). And as the migration spread further and further to the north, a brand new selection issue began to influence

So here's a clear demonstration that there is often no clear "good" or "bad" about a mutation — it may all depend upon the situation. These selective pressures are largely responsible for the magnificent diversity in modern human skin pigmentation.

Lynn Fancher, Associate Professor of Biology at the **College of DuPage** in Glen Ellyn, IL. “About Mutation”. 5 March 2012 <http://www.cod.edu/people/faculty/fancher/Mutation.htm>

Evidence #5: All humans have hundreds of potentially harmful mutations that they have acquired.

How Much Of A Mutant Are You?

Do you ever wonder how many harmful mutations you carry in your genome? Even if you've never worried about how much of a mutant you are, geneticists have spent a lot of time thinking about this issue. They are interested in a) how much genetic variation is out there, and b) how much of that is potentially harmful and connected to disease? This month's issue of *Genome Research* has some new research on an individual's personal mutational load.

By comparing the genomes of vertebrates, a group at Washington University found that the typical human genome probably carries between 800 and 900 harmful mutations, many of which are rare in the population. The idea of this research was to develop a method that will look at your genome sequence and predict which of your many genetic variants are likely to be harmful. The prediction method is still fairly primitive at this point, but multiple lines of evidence indicate that we all probably carry 100's of rare, harmful mutations.

A group from Arizona State also has some results in the same journal issue. They also have a method for predicting harmful mutations, and this method also relies on sequence conservation - that is, the method is based on information we get by taking evolution into account. Evolution isn't just something to irritate Biblical fundamentalists - it's a powerful source of information that's essential to making sense of our genomes.

So how close are we to looking at your personal genome sequence and telling you which genetic variants are likely to be deleterious to your health? Not very - these methods aren't yet ready for commercial prime time, but impressive progress has been made.

What I find most interesting (if somewhat obvious with hindsight), is that we all carry around a significant batch of potentially harmful mutations. Most of these are recessive anyway, with small if any effects on your health. Which means that there is another hurdle to overcome after we get better at predicting which variants are potentially harmful: which ones are actually harmful, that is, which are recessive, which ones have negligible effects, and which have large effects.

These types of questions are tackled in another paper in this issue of Genome Research, written by a group at The Scripps Research Institute. Recently cancer genomes have come in for some intensive sequencing, and now the challenge is to identify which mutations in cancer cells actually contribute to the progression of cancer:

Analysis of the frequency of specific mutations across different tumors has been able to identify some, but not all of the mutated genes that contribute to tumor initiation and progression. One reason for this is that other functionally important genes are likely to be mutated more rarely and only in specific contexts. Thus, for example, mutation in one member of a collection of functionally related genes may result in the same net effect.

Micheal White. How much of a mutant are you? 6 March 2012
<http://www.science20.com/adaptive_complexity/how_much_mutant_are_you>