Lesson Title: Freak-Genomics

Grade Level: 9-12

Time Allotment: 2-3 45 minute class periods

Overview
In this lesson students will enter the world of the genome, learning about human history and evolution by examining information about human, Neanderthal, and chimpanzee DNA. Using web interactives and video segments from the PBS series *The Human Spark,* students will be introduced to the ambitious Human Genome Project, learn about the genetic similarities and differences between human beings and our hominid ancestors, explore how specific genes manifest themselves in different organisms, and discover how genetic information can help us trace a path of human migration all the way back to our earliest ancestors.

This lesson is best used with students who have already learned about cellular structure and function in biology class, as well as with students who are already familiar with Darwin's theory of human evolution.

Media Resources
Journey Into DNA
http://www.pbs.org/wgbh/nova/genome/dna_flash.html
This interactive from the PBS series NOVA explores the structure of DNA and the human genome.

Atlas of the Human Journey
https://genographic.nationalgeographic.com/genographic/lan/en/atlas.html
This interactive timeline from National Geographic provides a comprehensive overview of the major y-chromosome DNA and mtDNA haplotypes found in humans over the past 200,000 years.

The Human Spark: Becoming Us**,** selected segments

Ratty Old Genes
This clip explores the extraction and interpretation of Neanderthal DNA.

Talk of Life
Using the FOX P2 "language gene" as an example, this clip explores how similar genes evolve differently in different animals

Objectives
Students will be able to:
- Identify parts of the genome and key terms relating to the genome;
- Explain genetic similarities and differences between humans, Neanderthals, and chimpanzees;
- Define gene expression;

- Explain how genetic research helps track human migration over time.

Standards

Life Science

Content Standard C

THE CELL

- Cells have particular structures that underlie their functions. Every cell is surrounded by a membrane that separates it from the outside world. Inside the cell is a concentrated mixture of thousands of different molecules which form a variety of specialized structures that carry out such cell functions as energy production, transport of molecules, waste disposal, synthesis of new molecules, and the storage of genetic material.
- Cells store and use information to guide their functions. The genetic information stored in DNA is used to direct the synthesis of the thousands of proteins that each cell requires.
- Cell functions are regulated. Regulation occurs both through changes in the activity of the functions performed by proteins and through the selective expression of individual genes. This regulation allows cells to respond to their environment and to control and coordinate cell growth and division.

THE MOLECULAR BASIS OF HEREDITY

- In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kinds (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters") and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome.
- Most of the cells in a human contain two copies of each of 22 different chromosomes. In addition, there is a pair of chromosomes that determines sex: a female contains two X chromosomes and a male contains one X and one Y chromosome. Transmission of genetic information to offspring occurs through egg and sperm cells that contain only one representative from each chromosome pair. An egg and a sperm unite to form a new individual. The fact that the human body is formed from cells that contain two copies of each chromosome—and therefore two copies of each gene—explains many features of human heredity, such as how variations that are hidden in one generation can be expressed in the next.
- Changes in DNA (mutations) occur spontaneously at low rates. Some of these changes make no difference to the organism, whereas others can change cells and organisms. Only mutations in germ cells can create the variation that changes an organism's offspring.

BIOLOGICAL EVOLUTION

[See Unifying Concepts and Processes]

- Species evolve over time. Evolution is the consequence of the interactions of (1) the potential for a species to increase its numbers, (2) the genetic variability of offspring due to mutation and recombination of genes, (3) a finite supply of the resources required for life, and (4) the ensuring selection by the environment of those offspring better able to survive and leave offspring.

Before the Lesson/Prep for Teachers

Prior to teaching this lesson, you will need to:

Preview all of the video segments and websites used in the lesson.

Download the video clips used in the lesson to your classroom computer(s) or prepare to watch them using your classroom's Internet connection.

Bookmark all websites that you plan to use in the lesson on each computer in your classroom. Using a social bookmarking tool such as delicious.com or diigo (www.diigo.com) (or an online bookmarking utility such as portaportal) will allow you to organize all the links in a central location.

Introductory Activity

1. Start class with a brief review of the structure of DNA, genes, and the human genome. Ask students to log on to the Journey Into DNA interactive in pairs or groups, depending on how many computers are available. As students click through the interactive, ask them to look for the answers to the following questions and write the answers in their notebooks. (You can ask these questions aloud as the students click through the screens, or project them on a screen or write them on the board for the class to see.)
    - How many cells are in the human body? (*100 trillion*)
    - How many bases are in the human genome? (*3 billion*)
    - Where is the genome located in the cell? (*in the nucleus, except for the red blood cell*)
    - How many chromosomes are in the genome? (*46 – 23 pairs*)
    - How much of the DNA in the genome has a known function? (*3% - 97% of the DNA sequence does not code for proteins*)
    - How many bases are in a gene? (*anywhere from 100 – several million*)
    - Identify the four bases and how they pair with each other. (*Adenine pairs with thymine, cytosine pairs with guanine*)
    - What makes up a nucleotide molecule? (*sugar, phosphate, and base*)

    Give students approximately 10 minutes to complete the interactive. When everyone is finished, review the answers with the class.

2. Ask class, based on their prior knowledge and what they saw in the interactive, to come up with a working definition for "gene." (*Answers may vary, but should include something like "a unit of DNA that determines a specific trait or specific genetic information."*) Ask students to come up with a class definition of "genome." (*Again, answers may vary, but should include "all of the genetic material in an organism."*)

3. Explain to students that much of what we know about the human genome comes from the Human Genome Project. Tell students that the Human Genome Project was an international effort, sponsored by the U.S. Department of Energy and the National Institutes of Health that ran from October 1990 to April 2003. Goals of the project included identifying all of the approximately 25,000 genes in human DNA and determining the sequence of the 3 billion base pairs that make up human DNA. To accomplish these goals, samples of genetic material were collected from volunteers all over the world and sent to Human Genome Project collection centers, where scientists worked on sequencing and analyzing the DNA. The full sequence was first published in April 2003. Ask students what they think some of the benefits might be to conducting this kind of large scale project? (*Accept all student answers.)* Explain that by mapping the genome, scientists are hoping to better understand genetic predispositions to diseases such as breast cancer, cystic fibrosis, and liver disease. The mapping of the genome will also make it easier for scientists and doctors to share information and discoveries about particular genes and genetic disorders.

4. Tell students that the human genome is not the only genome that has been sequenced. In fact, as part of the original Human Genome Project, genomes of other organisms, such as mice and the *e. coli* bacteria were sequenced and analyzed both to help develop the gene mapping technology and to learn more about interpreting gene function. Now that the technology for sequencing and interpreting the genome is in place, scientists are studying the genomes of organisms that can help us to learn more about human ancestry and evolution – chimpanzees and Neanderthals. By viewing and comparing the results of the Human, Chimpanzee, and Neanderthal Genome Projects, scientists can piece together a sort of "Rosetta Stone" of genetic changes and evolution since humans last shared a common ancestor with chimps six million years ago.

Learning Activity 1

1. Tell students that the majority of work on the Neanderthal Genome Project was done at the Max Planck Institute in Leipzig, Germany, where a team of scientists and biologists extracted DNA samples from Neanderthal remains found in Vindija Cave, Croatia. Tell students that you are going to show them a video clip explaining some of this team's work. Ask students to note, ask they watch the clip, the major genetic differences between Neanderthals and modern humans. Play clip, "Ratty Old Genes." When clip is finished, ask students to share their answers to the question, "What are the major genetic differences between Neanderthals and modern humans?" (*It's a trick question – according to the clip, there are* NO *major genetic differences!*)

2. The genomes of modern humans and Neanderthals, as well as chimpanzees, are overwhelmingly similar. Draw the following table on the board, or project it on a screen for the class to show the similarities between the three genomes:

Species	Chromosomes	Base Pairs
Human	46 (23 pairs)	approx. 3 billion
Neanderthal	46 (23 pairs)	approx. 3.2 billion
Chimpanzee	48 (24 pairs)	approx. 2.8 billion

Tell students that when comparing genome sequences, humans and Neanderthals share 99.7% of base pairs, and humans and chimpanzees share 98.5% of base pairs.

3. Comparison of the human genome to the chimpanzee and Neanderthal genomes may help to identify features that set anatomically modern humans apart from other hominins. It may also be helpful in tracing the path of human evolution. By comparing modern human DNA and Neanderthal DNA scientists can identify genes that may have changed or evolved since humans and Neanderthals diverged from their common ancestor approximately 500,000 years ago. We know from the video clip that there are very few genetic differences between humans and Neanderthals, but just how few? According to the published report from the Neanderthal Genome Project, which can be found here, if students are interested, there are only 78 – out of three billion! – instances of single letter nucleotide changes between present day human DNA and Neanderthal DNA. In these instances, the Neanderthal genome was in the same state as the chimpanzee genome, called the "ancestral state," whereas the present-day human genome had changed.

4. Although scientists can identify the single-letter nucleotide changes between Neanderthal DNA and modern human DNA, they have not yet been able to identify how these minute genetic difference translate to physical differences between Neanderthals and humans. In studying and making comparisons between Neanderthal DNA and human DNA, scientists did find evidence of gene flow from Neanderthals to humans, meaning that traces of Neanderthal DNA and sequences found in the Neanderthal genome are also found in modern human DNA. However, the gene flow only occurs in one direction – no evidence of human DNA has ever been found in any Neanderthal DNA samples. Again, it is unclear how this contributes to our modern human physical characteristics or knowledge about human evolution. The traces of Neanderthal DNA that do appear in the human genome occur randomly rather than consistently, which does not indicate any sort of evolutionary pattern or benefit.

5. Human and chimpanzee genomes are compared in different ways but still display striking similarities. When looking at the two genomes scientists don't just compare the single letter sequences but take into account all of the insertions, deletions, duplications, and rearrangements in the sequences. Even with all of this information the two genomes are close to 96% identical, and 29% of the genes found in the two genomes are completely identical. There are signs of evolution over time from the chimpanzee genome to the human genome – over 50 genes from the modern human genome are completely or partially missing or deleted from the

chimpanzee genome, suggesting the development or evolution of new genes and traits over time – but scientists have yet to pinpoint the exact significance of many of these changes.

Learning Activity 2

1. Explain to students that one of the anticipated benefits of the Human Genome Project, as well as having the Neanderthal and chimpanzee genomes for comparison, is that we can isolate specific genes and through them learn about human evolution and development, behavior patterns, and response to diseases and environmental stimuli.

2. Review the concept of gene regulation with class: certain genes in a cell can be turned on or off – expressed or repressed – in order to carry out a particular purpose or function. For example, in humans, each cell in the body contains all of the same genes and the same genome, but different genes are expressed in each cell, which is why we have different types of cells in our body – some cells "turn on" the genes to be skin cells, some are brain cells, some are stomach cells, etc. Gene expression is regulated by both signals from inside the cell and external factors such as interaction with other cells, proteins, temperature and other environmental conditions. This interaction between the genome and the internal and external cues dictates everything that happens during a cell's life. Scientists know that gene regulation is an essential function, but are not sure what makes the process happen.

3. Explain that while we know that genes turn themselves on and off in different parts of the body – the gene that gives you freckles in your skin cells has no need to turn itself on in your pancreas – scientists are exploring how genes express themselves differently in different species. The differences in how a gene expresses in a chimpanzee, Neanderthal, and a human may explain significant evolutionary differences and changes between the three species. Tell students that you are going to show them a video clip focusing on one such gene that expresses very differently in different animals, unofficially known as the "language gene." Write the following questions on the board or project them on a screen and ask students to write the answers in their notebooks as they watch the clip:
    a. What is the "language gene" called? (*Foxp2*)
    b. Name at least three animals that have this gene. (*fish, mice, chimps, humans*)
    c. What happened to the mice with the human form of this gene? (*they had a lower-pitched squeak*)
    d. Is the chimp version of this gene more similar to the human version or the mouse version? (*the mouse version*)
    e.

    Play clip, "Talk of Life." When clip is finished, review questions and answers with class. Explain that scientists are still trying to determine what internal and external factors turn the Foxp2 gene on, and how it affects speech once it is turned on.

4. The Foxp2 gene is of special interest to scientists for several reasons – language may be what sets us apart from our earlier hominin ancestors, and has allowed us

to communicate and organize as a society – but it is not certain yet it the gene is essential to "the human spark." Tell students that while the Foxp2 gene is different in humans and chimpanzees, as they saw in the video clip, recent research indicates that the Neanderthals possessed the same version of the Foxp2 gene that modern humans have today. Tell students that scientists are trying to figure out if this means that Neanderthals had the same capacity for speech as modern humans. Split the class into two groups, assigning one group to argue for Neanderthal speech capabilities, and the other group to argue against Neanderthal speech capabilities. Based on what students have learned about the minor genetic differences between humans and Neanderthals, as well as what they know about how genes express differently based on internal and external factors, ask each group to formulate a basic thesis supporting their assigned argument. Give each group 10 – 15 minutes to discuss, and then present to the class. (*Sample arguments FOR: the genetic differences between the two species are so minor that we could speculate that the gene would "turn on" the same way as in humans, anatomy is so similar that the same genetic expression would likely result in the same physical expression. AGAINST: Since the repercussions of the genetic differences are unknown we can't know if the Foxp2 gene would express in the same way, just because the gene is the same doesn't mean the expression would be the same – the mice in the video clip didn't start talking just because they had the same gene.*) Depending on the time and resources available to you and your class, you may wish to extend this activity, and have students spend more time researching this topic in the computer lab or library, and present their arguments in a debate setting.

Culminating Activity

1. Tell students that information from the genome can also help us track the spread of human populations across the globe as well as biological evolution. The prevailing theory for the spread of modern humans, called the "Out of Africa" or the "Recent Single Origin" theory, states that anatomically modern humans evolved solely in Africa between 200,000 and 100,000 years ago, and members of one branch of the population eventually left Africa and spread out across the world, replacing earlier hominid populations (such as Neanderthals). Scientists and genealogists are able to track the movement of this group, as well as splinter groups and populations through information found in the genome.

2. By using this information, many scientists and genealogists believe that all modern humans can trace their lineage back to a single common ancestor (or group of common ancestors) in Africa that lived between 100,000 and 200,000 years ago. They are able to do this by tracking two specific types of DNA that do not combine with any other DNA, thus passing from generation to generation virtually unchanged, with the exception of random mutations. These types of DNA are Y-chromosome DNA (yDNA), found in the sperm cell and passed down from father to son, and mitochondrial DNA (mtDNA), found outside of the cell nucleus and passed from mother to daughter. As time goes on, the random mutations are passed down over several generations and become inheritable genetic markers. This combination of genetic markers in an individual is called a *haplotype*, and population groups that all share the same haplotype are called *haplogroups*.

3. Ask students, in pairs or groups, to log on to the Atlas of the Human Journey interactive at the National Geographic website. Explain that several years ago National Geographic launched a project, similar to the Human Genome Project, collecting samples from volunteers all over the world, collecting genetic information to identify genetic markers and track human migration throughout history. Ask students to click on the "60 – 55,000 B.C." section of the timeline. Ask each pair or group to click on one of the six lines on the map: L0, L1, L2, L3, M*, or M1, read the information about their line, and answer these three questions:
   - When did this haplogroup first appear?
   - Where did this haplogroup first appear?
   - Where members of this haplogroup now?

   Give students approximately ten minutes to complete the activity, and then tell them they can have another five to ten minute to explore the interactive on their own. Ask them to think about the "Out of Africa" theory in mind as they click through the interactive, and think about how the growing and spreading human populations might have encountered Neanderthals or other early hominids as they migrated to other areas of the globe. Do students think the human populations would have faced challenges or difficulties? Do they agree with the "Out of Africa" theory?

4. If the "Out of Africa" theory is indeed accurate, and the modern humans did replace the early hominid populations…how did they do it? This brings up an uncomfortable subject for many scientists who are opposed to the idea of any interbreeding between anatomically modern humans and Neanderthals. However, many other scientists believe that genetic evidence indicated that interbreeding must have occurred. Comparisons of Neanderthal and modern human mitochondrial DNA does not appear to indicate interbreeding, while regular nuclear DNA analysis indicates the opposite – it's easy to see why scientists disagree!

5. The Neanderthal Genome Project team at the Max Planck Institute found what they consider to be evidence on the side of at least some interbreeding between Neanderthals and modern humans. When Neanderthals existed, they lived exclusively in Europe, Asia, and the Middle East. In studying and comparing Neanderthal and human DNA, the scientists found that any present day human whose ancestral group originated in one of those geographic regions shared between one and four percent of the Neanderthal genome, which would seem to indicate some interbreeding. At the same time, no present day humans of African ancestry shared any percentage of the Neanderthal genome – as their ancestors never would have come into contact with the Neanderthals. If, indeed, there was interbreeding, as the Max Planck Institute scientists suggest, they believe it would have happened at least 45,000 years ago, in the Middle East, before the divergence of the human populations across the Eurasian regions.

6. For homework, ask students to select one of the following three writing prompts, and write a one-to-two page essay:
   - Consider the Human Genome Project and its efforts to understand genetic disorders, diseases, and other intricacies and peculiarities of human DNA.

What do you think scientists could learn by studying the DNA of specific haplogroups or population groups? What are the potential implications of scientists using genetic information to classify people based on ethnic heritage?

- Presently, scientists disagree on whether or not Neanderthals and modern humans interbred during the time they co-existed in Europe, Asia, and the Middle East. Do you believe the there was interbreeding between the two species? Why or why not? How might this have affected the way modern human populations spread across the globe?

- In the Genographic Project, scientists isolated specific genes to trace human evolution through paths of migration from one location to another. At the Max Planck Institute, scientists isolated the Foxp2 gene to trace hominin evolution through the development of language. Imagine you are a scientists, and you can choose a specific type of gene to help you trace the path of human evolution over millions of years. What would you choose? Why?