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This Means War! The Battle of Humans and Viruses

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by Troy J Holiday

Overview

In today's world, obtaining success can be very competitive. This is especially true, because students increasingly have to compete with peers abroad as well as locally. Moreover, because of the state of the economy around the world, there seems to be more working age individuals than there are jobs. In days past, this wasn't the case; instead graduating from high school, let alone college, would almost guarantee you a way to earn good money in some capacity. Jobs were plentiful, and there was surely less competition. It's troublesome to think that, today, young adults are finding it harder and harder to find their choice of careers, even after earning a college degree. Consequently, it's more important than ever, that we as teachers do what we can to prepare our students for the hypercompetitive world that they will one day encounter.

With that in mind, I've chosen viruses and human evolution to be the topic of my unit. I chose viruses because it is becoming more and more evident that microbes and humans share a very close relationship. Microbes are extraordinarily talented and diverse, often performing multiple tasks while also living in a variety of situations. Furthermore, viruses have had a major impact on human evolution, and many recently published research articles seem to point towards a continued impact on our evolution in the near future. Evolution in itself is always a polarizing topic with my students, since it brings into play people's belief systems and ways of life. In general, people seem to become very passionate when their beliefs or ways of life are challenged, and for my students that idea holds true. I hope to shine a light on this connection and explore with my students the role that viruses played in our evolution and where the viruses might lead us in the future. This will be done with examples of these relationships in the past, present, and future. Science fiction examples will also be included, to help bring levity and creativity to the unit.

Students of today, like microbes, are not lacking in talent and diversity. They are varied in terms of age, prior education, and particularly, motivations. I teach Biology at South Philadelphia High School, in Philadelphia PA. My student population at the school is very diverse culturally; however, with regards to class or social status, they are all about the same. The school is in an urban setting, causing my students to be often exposed to things that a normal teenager would not encounter. Therefore, when teaching my students anything Science related, I make sure to make the information as relevant as possible, by frequently asking them to characterize the lessons in their own words along with identifying how the lesson relates to their own lives. I have experienced success with this method because it allows students to take ownership of what they learn.

In particular, scientists have found that viruses played a crucial role in human evolution, providing us with characteristics derived from virus genes, which help us to survive and reproduce. Despite the lack of focus on these concepts, my unit will align with the following Pennsylvania science standards:

3.1.B.B1 3.1.B.B3 3.1.B.C1 3.1.B.C2 3.1.B.C3

More detailed explanation of the standards can be found in the appendices

While the standards touch on the basic principles of how viruses work, they don't achieve the goal of sparking my student's curiosity. Ultimately, I want my students to be inspired to learn more about the topic of virus and human relationships. Viruses and humans share a story that is steeped with drama. The war has been playing out since the beginning of human existence with both sides relentlessly trying to out duel the other. Understanding this story requires my students to thoroughly investigate the background of virus-human relationships. Accordingly, this will be followed with an analysis of the current day status of the relationship, in addition to a predictive component that encourages students to hypothesize about the future relationships between viruses and humans. In addition, my students will become aware of the many careers that are emerging out of the field of microbiology. Careers in fields such as: Biotechnology, Pharmaceuticals, Science Education, Science Writing, Graphic Design for scientists, or even the possibility of combining their knowledge with Business or Law degrees. These industries and more are now possible because of recent advancements in our understanding of microbes.

In order to successfully engage my students in the unit, they must be able to form an opinion about the topic. To create debate amongst my students, I plan to teach specific skills. Skills like, critically analyzing information, forming an argument, and finding scientific evidence to defend an argument. They will accomplish this by focusing on these following objectives:

1. Understanding the general impact and significance of viruses on our planet.
2. Identifying the role that humans play in our relationship with viruses.
3. Hypothesizing about the relationship between humans and viruses in the future.

These objectives join together to paint the picture, or tell the story of the never ending process of evolution on our planet. More specifically, these objectives attempt to explain the fragile nature of life and the desire of two of the planet's most successful organisms to survive and reproduce. Using the objectives in this way should help reinforce the major concepts of the relationship, and help motivate my students to explore the subject further.

Objective

Like most states in the USA, my state of Pennsylvania has very specific standards about how to teach Microbiology. However, much of what we do just scratches the surface of what could be covered in this branch of Biology. It usually involves many lessons on the characteristics of the cell. This usually leads us to lessons on heredity and the details of how genes pass from generation to generation. Unfortunately, when it comes to the world of microbes, very little information is provided on the vast complexities that make up this hidden world. Because of this, my unit reinforces the importance of microbes and the roles they play in our everyday lives. Specifically, my students will understand the relationship that exists between viruses and humans.

In fact, the Science Standards for the state of Pennsylvania, barely list any standards that apply to microbes, let alone viruses. The standards that do apply to microbes, barely focus on the important concepts of microbes and instead briefly mention their significance as part of a more "important" concept like, ecosystems or human physiology. From what we now know about the significance of microbes, it seems like our current practices provide a great disservice to our students. The field is so dynamic and rich that scientists now believe our new understanding of microbes could be a game changer in the field of biology, shining new light onto our place and purpose in the world.

Background

There is a vast amount of microbes that exist in our world and yet, most of them seem to lack the level of disdain that surrounds the reputation of viruses. While various protozoa, bacteria, and fungi share many of the same qualities as viruses, they don't quite seem to strike the same type of fears in us as viruses do. This is probably due to the fact that many viruses cause serious illness in humans and domesticated animals, as well as inflict damage on crop plants. The shared relationship that microbes and humans possess has long been known. However not until relatively recently, have we discovered just how close our relationship has been. There is a large amount of research that suggests the evolution of our species is directly connected to the evolution of viruses.

With this in mind, I believe it is critical for my students to understand the significance of viruses in our world. By my students achieving this level of understanding, they will reinforce many of the major themes learned throughout the year in Biology. This includes, most importantly, being able to identify viruses' role in this constantly changing world and how science can be used to validate viruses' significance in our civilization.

Furthermore, it will help my students to see that while viruses do cause disease, they can also be useful as tools for our survival. This should prepare them for any encounters they may have in their lives with viruses, which is important since the war between humans and viruses seems to have no end in sight.

Virology History

Before any progress is made in the unit, my students must explore some of the fundamentals of Virology. They must then apply what they learn to the impact viruses have had on human civilization. It was only 100 years ago that viruses were shown to be filterable and therefore distinct from bacteria as possible agents of infectious disease. Before this point we were not exactly sure what caused our diseases and infections. There were many hypotheses and beliefs about what could explain the various maladies we experienced, some very close to what we understand today about viruses, and others that were completely off base. It wasn't until 60 years ago that the composition of viruses was described, furthering our understanding of what a virus is and what a virus does. Within the last 20 years, however, the revolution of modern biotechnology has led to an explosive increase in our knowledge of viruses and their interactions with their hosts. Over this time, our perception of viruses has changed so much that now there is an increasing movement towards viewing Viruses as tools of study that can increase our chances of survival. Viruses have also provided a great service by allowing us a deeper understanding in the fields of gene cloning, and interactions of viruses with the immune system; in a sense, these studies tell us as much about human biology as the work has told us about the viruses themselves (James H. Strauss 2002).

Virus Life Cycle

In order for viruses to survive they need a host. This by nature makes a virus a parasite. Their entire existence is directly connected to their ability to find a host that will allow them to proliferate. For this to happen, a virus must infect a host and take over the cell or cells to produce more virus copies (James H. Strauss 2002). When a host cell is infected, all of its metabolic functions are then taken over for the purpose making virus copies. Once the cell is hijacked to begin the process of replicating more copies of the virus' genes, it is also instructed by the virus to create additional viruses that will exit the cell and infect other nearby cells. This is accomplished by releasing the virus genome into the cytoplasm of the cell, instructing the cell to replicate the virus genome to make more viruses. The point of a virus, like all organisms, is to survive and reproduce; thus, viruses have evolved ingenious methods to accomplish these tasks.

The first characteristic of a virus that makes this possible, is that most viruses encode enzymes required for replication of the genome and the production of mRNA. The next thing that must occur is the production of proteins. But not just any proteins, these are specific proteins that are made within the cell and used to assemble progeny viruses. These specific proteins may be coded in the virus genome, or coded by genes that already exist in our own genome (originating from genes that entered our genomes long ago in human evolution) or they target more complicated proteins that are required for virus assembly but do not exist in the virus' genome. Thirdly, many large viruses can code for proteins that block defense mechanisms of the host, making it easier for the virus to integrate into the host cell. This strategy prevents our highly evolved immune defense mechanisms from eliminating the virus infection, and prevents the host cell from recognizing the intrusion of foreign DNA (James H. Strauss 2002).

Classification of Viruses

The classification of viruses largely depends on the genome of the virus and how it replicates, in addition to the virus' morphology (what the virus look like). To avoid spending too much time discussing the various ways in which viruses can differ, I will focus on highlighting the most crucial differences. More information on the classification of viruses can easily be found online or in books that specialize on the topic. Viruses can essentially be broken down into 3 broad classes, with each of them possibly having independent origins of evolution. One class, which includes the poxviruses and herpesviruses among many others, contains DNA as the genome, whether single stranded or double stranded, and the DNA genome is replicated by direct DNA → DNA copying (James H. Strauss 2002). The herpesviruses have benefited greatly from this characteristic giving them the ability to remain in the human body undetected by our immune systems for an entire human lifetime. More details on the herpesviruses will be discussed later in the section.

In contrast, the second class of virus contains RNA as the genome and the RNA is replicated by direct RNA → RNA copying. Viruses of this sort tend to have a more difficult time infecting a host, since virus-encoded proteins are required to form a replicase (enzyme for replication) to replicate the Viral RNA, since cells do not possess (efficient) RNA → RNA copying enzymes (James H. Strauss 2002). Because this class of virus has extra obstacles to overcome, it would seem as though these particular viruses would not be as virulent, or deadly, as others. However, because this class of virus has an RNA genome, it also experiences a much higher rate of mutation than would a DNA virus. Accordingly, the high mutation rate of RNA gives it a better chance to make genetic variants that can be naturally selected to survive, sometimes producing strains of virus that our bodies are completely unprepared to fight off. This was the case for the yellow fever epidemic that has been plaguing our society for centuries, if not longer, costing hundreds of thousands of lives throughout our history.

The third class of viruses encode the enzyme reverse transcriptase (RT), and these viruses have an RNA → DNA step in their life cycle. The genetic information encoded by these viruses thus alternates between being present in RNA and being present in DNA. This class of viruses is of particular importance to this unit because of its versatility and virulence in our world. You will find that, this class of virus is often referred to as a Retrovirus, named so because of the way it replicates in its host. More specifically, it replicates through the process of reverse transcription, using the reverse transcriptase enzyme to produce DNA from an RNA genome. This is opposite to the outdated 'central dogma' (assertion that RNA can only come from DNA), hence the origination of 'retro' (backwards) in the name retroviruses. These types of viruses are unique to all other viruses and can be very hard to eliminate because of their high mutation rates and the fact that they possess the ability to integrate into human cells and avoid detection by our immune system (James H. Strauss 2002).

Replication Cycles

The replication cycles of viruses also help to distinguish them from each other. The first task a virus has to accomplish, before replication can begin, is entry into the cell. During this stage viruses will bind to receptor sites on the cell if the correct protein interaction is or is not available to initiate the binding and infection process. Binding usually occurs in several steps. Some receptors on cells exist in high concentrations, and others do not. Thus, it behooves a virus to evolve a structure that matches with receptors that are most abundant. With this in mind, it shouldn't be surprising that viruses have evolved, through natural selection, to use receptors that are the most abundant on cells (James H. Strauss 2002).

Penetration

Once the virus has completed the necessary stages for binding to a receptor on a cell, the next stage required for successful infection is the introduction of the viral genome into the cytoplasm of the cell (James H. Strauss 2002). This can occur in various ways, all of which have to integrate into the basic functioning of the cell. Some cases involve a subviral particle containing the viral nucleic acid (DNA or RNA) being introduced into the cell. Other cases involve only the nucleic acid being introduced.

For enveloped viruses, penetration into the cell involves fusion of the envelope of the virus with a cellular membrane. When this occurs, a dramatic rearrangement of proteins allows for receptors to fuse with the virus envelope and permit entry into the cell. This method has proven to be very efficient, demonstrating in some well-studied cases almost all particles succeeding in initiating infection (James H. Strauss 2002). For viruses that lack an envelope the process seems to be a bit unclear. However, the general belief is that a rearrangement of structure is initiated by the binding of the virus to the receptors.

Replication and Expression of Virus Genome

There are many more detailed steps that take place during the replication cycle of viruses that I will not describe in this unit. However, before I move on from replication, I will briefly explain what happens after a DNA virus enters into the cell for replication, since much of the unit focuses on DNA viruses.

The first thing that should be noted is that after entry into the cell the virus DNA will be transported to the nucleus, or control center of the cell. There it is transcribed into mRNA by host RNA polymerase. Viral mRNAs are then translated by host ribosomes in the cytoplasm, and newly synthesized viral proteins are transported back to the nucleus. After the DNA genome is replicated in the nucleus, either by host DNA polymerase or by a new viral-encoded polymerase, progeny virus particles are assembled and ultimately released from the cell (James H. Strauss 2002).

Rationale

With all the vast amount of ways that viruses have evolved to infect our cells, it's no wonder that viruses have been highly successful in surviving and reproducing within humans. However, it is also amazing how successful we humans have been in fighting off these viruses. This evolutionary dance of mutual co-evolution that has been taking place between humans and viruses has been happening since our species first evolved on this planet. There are many reasons as to why this back and forth between humans and viruses has taken place. Much of it has been attributed to our "rendering of the fabric of our environment, changing our behavior, and ironically, by our inventiveness in increasing the length of quality of lives." (Karlen 1995). Essentially, what some believe, is that by constantly changing and adapting to survive, we humans have created the conditions that we live in today. To use colloquial terms, we've made our bed and now we must sleep in it. The shared evolution of humans and microbes has accelerated to a frenzied pace, because of changes we made in our environment and lifestyle.

Our changes to our environment pretty much come from two hardwired imperatives that, at the end of the day, every living thing possesses: the desire to survive and reproduce (Dr. Sharon Moalem 2007). Our need to survive and reproduce has led us to constantly experience evolution, which is simply defined as the change in genetic makeup of a population through time. Sometimes when we think of evolution we think of the process of genetically changing from primate ancestors to modern man. However, evolution and adaptation can often take place on a much smaller scale than species formation, and in fact with most cases it does. Currently, scientists refer to this phenomenon as an "Arms Race" between species or the "Red Queen Hypothesis". Ultimately, they describe this phenomenon in this way to illuminate the parallels with the Red Queen, a character in Lewis Carroll's *Alice's Adventures in Wonderland*. The Red Queen tells Alice, "...It takes all the running you can do, to stay in one place.", and this ongoing relationship is typical of host-pathogen interactions such as between humans and viruses. The more evolutionary advantage we gain against viruses, the more they seem to evolve better counter attacks, so that no matter how much progress we make we seem to end in the same place we started.

The truth is that we have been evolving in tandem with all of these microscopic organisms- sometimes to our benefit and other times to our detriment. The way our bodies work today is directly related to our interaction with infectious agents over millions of years. Some theories even pose that sexual attraction has a connection to disease. For example, it is believed that the smell of someone you find sexually attractive is often a sign that you have a dissimilar immune system, which will give your children wider inherited immunity than either of their parents (Dr. Sharon Moalem 2007).

Mechanisms of Evolution

One of the most prominent biologists of our time said that, "No organisms are evolving faster with more consequences than are the parasites among us" (Ewald 1994). This biologist is Paul Ewald and he continues to give talks and conduct research on the evolution of infectious disease. Ewald's statement highlights an important point about the nature of microbes. Their evolution, and in particular the evolution of viruses, is something that we should all be mindful of since much research suggests their evolution is directly tied to our own. We are also discovering it's not just humans and viruses that are tied together by evolution, in fact, "To be crystal clear: everything out there is influencing the evolution of everything else" (Dr. Sharon Moalem 2007)

Ironically, in the midst of this merciless war between viruses and humans, we have been brought closer

together as opposed to driven further apart. There is growing research that supports this idea of symbiosis. This is the idea that two organisms can have a long-term relationship with each other. Recent research has posed that the close relationship between humans and viruses has given both of us benefits for survival. The reason this concept is taking such hold on the scientific community is because the evidence of these types of relationships are being discovered more and more frequently.

One leading science writer, Carl Zimmer, explores the idea of introgression, essentially the movement of a gene from one species into the gene pool of another, and speaks about one example in particular that is more familiar to us. It is now accepted that mitochondria organelles (aka power plants) in our cells, are derived from bacteria that once existed millions of years ago and became symbiotic with the cells of eukaryotes such as humans. Recent research from French biologist, Jonathan Filee and Patrick Forterre, has suggested that the mitochondria also possess genes from viruses. Mr. Zimmer explains that, "The invading virus's DNA simply became a harmless part of its host's genome. In many cases, the genes of cryptic viruses have suffered major damage from later mutations and many of their genes have been cut out of their host genomes altogether "(Zimmer 2005). This might help us explain why it might have taken so long to discover this type of DNA in the mitochondria.

The research is fascinating and tantalizing to say the least. "It suggests that we are chimeras built from the DNA of eukaryotes, bacteria, and viruses, all mixed together through a natural version of genetic engineering"(Zimmer 2005). If this is true, then we must reevaluate how we assess our past and who we are as individuals. The old adage states, "you have to know from whence you came, to know where you are going." Accordingly we must now look through a different lens to understand where we came from and where we are headed. Zimmer goes on to say, "Forterre even argues that these sorts of results are going to turn out to be the tip of the iceberg. Like many scientists, he believes that before life was based on DNA, the Earth was inhabited by RNA-based life. He argues that DNA was an invention of viruses of these RNA-based organisms, which the RNA-based organisms then seized for their own use"(Zimmer 2005).

So it should be clear why I compare the human-virus relationship to war. The constant rate of adaptation we have discovered lets us know that this war is far from over. Especially, when we take into consideration the rate at which mutations are taking place. Some may view our situation as dire or doomed to fail; however maybe we are just using the wrong perspective. If we can somehow learn from viruses about how to be more efficient at surviving, then maybe we can extend our lifetimes and learn to live in harmony with the viruses that vastly outnumber us in this world. If you can't beat them, join them, is what they say and maybe that's the case for some of our more virulent viruses. Unfortunately, we know that in many cases the only option for our well being, is eradication of a virus that causes serious disease in humans, such as smallpox. I believe Arno Karlen said it best with this statement, "They like us, are trying to adapt and survive. Some must be conquered, some require a wise truce"(Karlen 1995). Identifying which virus deserves which treatment is the key, and maybe the most difficult task to achieve, but I guess these are the trials and tribulations of war.

When engaged in any warlike scenario, the first thing to understand is who you are fighting. Additionally, we should begin to understand that species, in general, are designed and crafted through natural selection to fit perfectly into their space in nature. Therefore, when you look at each organism that inhabits their niche naturally, you begin to understand what characteristics they possess that allows for them to survive there. Accordingly, the fit of an organism to its environment is the result of its history, the action of natural selection gradually modifying populations over the course of time(Marks 1995). The mutations that an organism possesses are what allow them to survive, so one would think that the reason mutations happen is so that we can adapt and survive in our environments. However, that is not the case. In fact, mutations have no purpose

at all. Mutations happen often, very often to be precise; it is just that most of them we don't see or are just not recognized. This is because most mutations are neutral, having little to do with adaptation (Marks 1995). It just so happens that every once in a while a mutation will present an organism with an increased fitness for the environment, stimulating the process of evolution, and the ability for these mutants to take over the population.

If most mutations are neutral, why is that biologist's claim that all organisms we see today are some form of mutant, including ourselves? One reason is that most organisms of the same species share the same mutations, so they are harder to recognize. Another idea that helps put this in perspective is the massive amount of people that live on this planet. When that many organisms exist it opens the door for that many more mutations to occur. We are mutating often because we are reproducing rapidly, and any child could have a mutation differing from its parent's DNA. Something along the line of 100 billion mutations is produced each generation according to one study (Ervolino 2014). If each one of those mutations caused a significant change in our phenotype than just imagine how rapidly we would change each generation. It would be impossible to keep track of all the changes. It would also seemingly increase the chances that these mutations could lead to the extinction of our species, since we know that all mutations are not beneficial. It has also been suggested that, on average, each duplication of the human genome includes 100 new errors, leading to the question: why aren't we more different from our parents? It appears as though, while these many mutations do occur, sometimes these genes can become silenced or dormant, causing us no harm but waiting to be unlocked by an external factor from the environment (Ervolino 2014).

Recent discoveries have uncovered that 8% of our DNA comes from viruses and these may have helped us to survive since the beginning of our species existence. This strange twist to our war story has now changed how we view viruses. Some of that 8% of DNA has contributed to the mammalian development of the placenta, because these genes for placenta formation are definitely of virus origin. This vital mutation has allowed mammals, including humans, to survive throughout our evolution. In a way, this means that we would not be here if it were not for viruses, which means we owe them more than they owe us. The irony of that statement is one that I hope my students will be able to appreciate.

Future Applications

If we can revisit the idea mentioned earlier, on the mechanisms of evolution, we can learn much about what our future genomes may look like. Another leading biologist, who recently passed away, Lynn Margulis, had a fascinating idea about the true reason behind why we evolve. She argues that in life, "What begins as parasitism, ends in symbiosis". This is meant to imply that cooperation, or symbiosis, is the driving force of evolution (Karlen 1995). Furthermore, she argued that each organelle started as an infection, and each human cell is a community of onetime invaders. So then what does that make a virus?

According to her research, she believes that a virus is nothing more than degenerated bacteria that evolved from cellular organelles, perhaps from mitochondria that escaped to a semi-independent existence (Karlen 1995). She then goes on to suggest that interactions between parasites and hosts go through stages called, epidemic, endemic, and coming full circle to symbiosis. During the stage of symbiosis the organism can experience two different versions, mutualism or commensalism. During mutualism, they will both benefit from their relationship. If the organisms happen to experience commensalism, both organisms obtain a mutual tolerance for each other, hence the true meaning of commensalism being, "Dining at the same table" (Karlen 1995). I find this very interesting because it relates to what is happening with the relationship of viruses and humans at this moment in time. Hopefully, this will spark my student's curiosity to wonder about the

possibilities of the future and how our relationship will evolve from here. Today, we still do not know where viruses come from, but we are almost positive they are not degenerative bacteria. The common thought today is that they were around before we got here and have figured out a way to survive with the help of a host. Another theory is that through the process of evolution they split off into a reduced form of others forms of life, which possessed a bigger genome; this aligns closely with Margulis' idea. While each of these theories seems logical, if we don't approach viruses with an open mind our understanding may get stuck in place further reinforcing the concept of the "Red Queen Hypothesis".

Speculating about the future evolution of viruses and humans may seem trivial to some, after all we are probably a long ways away from any significant or noticeable phenotypic changes resulting from our interactions with viruses. However, with the possibilities being so vast and diverse, it is hard not to take time to hypothesize what could occur. The unfiltered minds of my students will revel in this opportunity. Therefore, in order to do begin this dream state of ours we can look at familiar viruses for inspiration.

Many of the ideas we know about today have been around for some time, more than 50 years in some cases. Take, for example, genetic engineering. It got its start in 1972, by geneticist Stanley Cohen and Herbert Boyer. It started with them using plasmids, small circular loops of extra chromosomal DNA, in which bacteria carry some of their genes(Naam 2005). The structures that deliver genes into a cell are called vectors and it should not be surprising that most natural vectors for delivering genes of use are viruses. Actually, penetrating a cell is one of a virus' main abilities, making it perfect for this role in the cell. A virus also already has the built-in hardware to complete this task since so much of its fitness depends on the host that it occupies.

However, just like with almost anything, there are some drawbacks. Sometimes the immune system can detect the virus, which could cause the virus to be attacked. The vectors are also not very precise, where often times the virus will just attach to whatever host cell's genome they can reach. This could be disastrous since it could potentially land next to a gene that is vital for survival (for example, a tumor suppressor gene). However, all that being said, as Bioethicist, Arthur Caplan, put it "The notion of enhancement is deeply ingrained in our culture", he continued to say, " we are not the end of evolution- there's no such thing", " we are, if we choose to be, the seed from which wondrous new kinds of life can grow. We are the prospective parents of new unimaginable creatures "(Naam 2005).

Future Examples of Virus Potential

As aforementioned, the unit will provide plenty of opportunity for my students to let their imagination run wild and speculate on the many possible uses of viruses. These moments will be enhanced by some of the examples we will discuss in class. When my students hear about the so-called, "superhero" viruses, they should become more curious about the role viruses play in our lives. The examples we will discuss will be relevant and familiar to them all, helping them to make the lessons we will cover more tangible.

The first example we will discuss is Herpes Simplex Virus. This virus' power resides in the subterfuge and stealth that it has evolved over time. Once acquired, this virus will last a lifetime with most of its life cycle being spent as a master of disguise, invisible to the world. It is said that 80% of the human population is infected, most unknowingly(Smith 2014). HSV is extremely ancient, giving credence to the idea that it has an extraordinary ability to survive as a pathogen alongside humans. Because all viruses need a host to survive, HSV has evolved a way to go undetected in the body, allowing carriers of the disease to transmit the infection without even realizing it.

But, how is this accomplished you might ask?

When the disease is first manifested it doesn't appear as a cold sore, instead you develop a severe sore throat, swollen lymph nodes and a high temperature. These symptoms represent your body responding to the infection. Then, before your body can attack the disease the nerve endings in your mouth serve as the "getaway car", which the virus uses to escape the war in the mouth. Rather than behave as other viruses and reproduce, it slips into the cell's nucleus, twists itself into a small circle of DNA and lies low. This is what is referred to as latency (Smith 2014). It could potentially hide in this location for the host's entire life undetected by the immune system. It's able to hide in this way, because it doesn't manufacture proteins, which would certainly give its location away. When it recognizes a trigger from the nervous system and jumps into action and reactivates, priming it to reproduce. My students should begin to understand that if humans could one day figure out how to adapt these types of qualities, then we too, could potentially possess superpowers.

The next example that students will explore is the effects of the Rabies Virus. This virus' superpower is mind control. Yes, mind control!

Rabies has the ability to colonize salivary glands of its host making it difficult to swallow. This in turn will cause foaming of the mouth, which is a widely known symptom of rabies. The next step of the process involves an infection of the brain, making the host feel higher and higher levels of agitation and aggression (Dr. Sharon Moalem 2007). When animals are agitated and aggressive they tend to bite. When their mouths are foaming with rabies-filled saliva their bites will cause infection; this allows the virus to survive and be transmitted. Survival and reproduction is the primary goal for any organism and rabies virus, has figured out a hell of a way to make this happen. One additional anecdote is that this might be where the idea of a Werewolf originated, with its roots in the ancient observations of the rabies virus at work. My students will be able to take this information and imagine what it would be like if humans adapted this ability to make the host feel higher levels of aggression and agitation.

Strategies

As mentioned earlier, the main purpose of my unit is to get my students to speculate about the future of human and virus relationships. I would like for my students to take what they have learned and use it to hypothesize the future evolution of both humans and viruses. To accomplish, they will have to understand many facts about virology, which is why so much information is included in the rationale and the background sections of the unit. The better they understand the topic, the better their hypotheses will be. Therefore, it will be critical for them and I to reinforce any other major ideas discussed, until we feel comfortable enough to move forward.

Clearly, this is much easier said than done. Much of what needs to be done to make this a reality occurs in the beginning of the unit. In order for me to sustain their motivation throughout the unit, I will have to hook them in during the beginning stages of this process. I have found that regardless of how exciting a subject may be to me, my students might feel otherwise. Therefore, when developing this unit, my first challenge was to identify what interests my students and how it all relates to viruses. It dawned on me that the history of humans and viruses told a story of winners and losers. Sometimes one side was victorious and then other times the opposing side would claim victory. This back and forth, between humans and viruses in particular,

has been taking place since the beginning of our existence.

For some reason, this sounded very much like the war stories I learned about in history and social studies class, or even the wars that we hear about in today's world. I was able connect this idea to the many discussions I've had with my students about wars, battles, and fights that they had come across. Therefore, from the outset of this unit, I decided that the central theme would be the war between viruses and humans.

Even though war is a topic that I know most students will enjoy, I didn't want to spend the entire unit focused on the history of humans and viruses. I was afraid that many of the lessons would end up seeming too much like history class, where most of what was learned focused on the dates, places, and events that propagated the war between humans and viruses. Instead, I wanted much more of the unit to focus on a predictive component, where the students will take what they learned and hypothesize about possible future worlds with humans and viruses. Ultimately this will lead to us reaching our culminating activity, which has the students create hypothesized worlds in the form of comic books.

Building up to this point will require scaffolding and the development of their understanding to prepare them for final project. This process will encourage them to learn about topics as they come up, giving them ownership over what they learn. This form of self-discovery should help to galvanize their confidence on the topic, and lay the foundation from which they will depend on throughout the unit.

The first day of this journey will begin with a simple game of "battle competition" between different animals. This will be the piece that hooks them into the unit. They will make predictions about who they think will win and why. Then, they will watch the video clip play out on YouTube, to test out their predictions. After each battle clip is completed, we will discuss as a class, what gave each animal an advantage over the other. The Animal Planet channel does a really good job of explaining each of these battles and what would give a particular animal an advantage over the other. This could serve as a great line of support when teaching this topic. The last battle I will display on the board will be of human vs virus. I expect students to be perplexed at first, wondering about the type of battle they are observing. This is when I will begin to introduce to them the raging war that has been taking place between humans and viruses since the beginning of our time on earth.

The next day we will begin to identify specific viruses and highlight the features that make them unique. The viruses we will observe will range from small to big, least virulent to most virulent, ancient to modern, and separate them based on their characteristics. Following that, the class will break up into groups. The groups will be split in half and given a particular virus to research. For example, if I have 6 groups in a class, I will give three groups one type of virus and the other 3 groups another type of virus. Inside of each of the sets of groups their responsibilities will be broken down even further so that each group in the set will be given an assignment to either research the past, present or future evolution of a virus. After the research is complete, we will all reconvene as a class and discuss what they have found. This should help them to understand how viruses differ and how closely they are related to human evolution.

As we move forward through the unit, my students should begin to gain a deeper understanding of the topic. Accordingly, we will spend the next day discussing the give and take relationship that humans and viruses share. The centerpiece for this discussion will be HIV/AIDS. In fact, to illuminate this relationship my students will group together and work on a case study that involves the virology of HIV/AIDS. The goal, again, is to enrich my student's knowledge of viruses and their relationship with humans; therefore I believe that by focusing on a virus such as HIV/AIDS, my students will have an easier time relating to the topic since it is one of the biggest epidemics of our lifetime. Ultimately, what they should take away from this activity is that, both organisms are just trying to survive and reproduce, which seems to be the main purpose of evolution. Other

factors that contribute to evolution will also be addressed, like population size and other environmental factors. If they can grasp these ideas, then it should become clear to them that viruses are very much conduits of gene flow, keeping the world in constant state of evolution.

The next day of class will introduce a brand new idea to my students. We will discuss some revolutionary news in science and talk about its significance. I will explain to them that 8% of our DNA is viral, and that some of the genes in the 8% are the reason we are here today. So my students will begin to understand, that we are, in fact, mutants that have joined forces with viruses to make us who we are today, giving new meaning to the phrase, "if you can't beat them, join them". They will use the new found knowledge and participate in, what we call, a Socratic Seminar to debate the future of the human-virus relationship. Using their facts and opinions they will debate what they believe the future of our relationship to be and support their arguments with facts that they have collected from the previous lessons. Some possible ideas to discuss are: who wins the war, what a full integration of human and virus DNA may look like, and the potential phenotypes that could arise from the mutation and integration of human-virus DNA.

During those 5 days my students will be building as much background knowledge as they can to prepare for the final, culminating activity. The 5 days that follow will engage my students in a project based activity that will involve all of the concepts we will have learned on viruses. The activity will involve my students creating a comic book that tells the story of the human-virus relationship. They will be given specific parameters to set the stage for how they will tell the story. I will encourage my students to think creatively and come up with ways to tell the story in a fantastical manner. Their stories will be hypothetical and build on their debate of the future of the human-virus relationship.

Getting started is often the hardest part of writing a story; therefore I will provide many examples of similar stories that have already been told. Examples such as television show *The Walking Dead*, and movies *I Am Legend*, and *X-Men* all deal with some type of post-apocalyptic event that caused a significant change in the human gene pool. Each story uniquely focuses on the theoretical outcomes, if such an event were to occur. Providing my students with these examples should inspire them to come up with their own version of the story. After generating their ideas, they will outline the plot of the story so that it can be peer reviewed. Following the peer review, I will check that the stories are aligned with the topics discussed in class and they will proceed to make their comic books. A rubric will accompany this activity to guide them through the process and ensure that they know exactly what is expected of them. The rubric will include the outline/concept map, spelling and grammar, research and writing, and creativity and it can all be found in the appendices of this unit.

I believe that ending the unit with this activity will be a lot of fun for my students. It will give them the opportunity to demonstrate their understanding of the concepts in a creative and engaging way.

Ironically, I believe that many of the ideas my students create, will be more feasible than many people would think. Which is what makes the topic so interesting and why many movies and science fiction stories have used these ideas at their foundation to explain our potential future. If my students understand the feasibility of many of their ideas, it could inspire them to pursue these concepts in the future. If nothing else, my students should take away from this unit the idea that, the human-virus relationship has had major impact on evolution on this planet, producing some of the most amazing marvels of our world. There is no reason to doubt, that if business continues as usual, we will see the development and creation of some of the more amazing things we can and cannot imagine.

Activities

HIV/AIDS Case Study

Objectives:

- Describe the symptoms related to HIV/AIDS and how a person is tested for HIV.
- Propose treatment targets for controlling HIV infection based on its life cycle.
- Speculate biological and immunological reasons for why HIV infected people are non-progressors and progressors.
- Describe molecular mechanisms of HIV drug resistance and molecular evolution.
- Determine the pros and cons for specific HIV treatment approaches.

Anticipatory Set

Class will begin with my students speculating on what they know about HIV/AIDS. They will be prompted to perform a quick write, where they will write continuously for 5-7 minutes on the topic of HIV/AIDS. During this time my students will be asked to write uninterrupted and to put whatever is on their mind, without any thoughts on the quality of their work. Following their writing, some students will share what they have written, after which, we will discuss it as a class.

Direct Instruction

The anticipatory discussion will be followed with me instructing the class on how the day's case study will be executed. I will start by describing what case studies are, and how they work. The case study will be a follow up to the information discussed throughout the unit, therefore my students should be fully prepared to engage in this particular study. It will be explained to them, that after they collaborate to discuss the case, they will regroup to share what they have learned with the class. Once I am comfortable that my students understand my expectations, I will proceed to pass out the assignment.

Guided Practice

The handout given to my students will explain the process the HIV/AIDS virus uses to enter and infect our cells. I will read aloud the handout to the class. They will take notes as they read along with me. In addition, I will point out any important points they will need for later in the activity. Once the reading is complete they will answer a set of questions that accompany the handout.

Independent Practice

My students will then answer each question individually making sure to apply what they've previously learned along with what information they got from the reading. Every group will be assigned a specific character from the case study with questions that are specific for their characters. When each member of the group has completed the questions, they will share out the questions and come to consensus on each question.

Modeling

Once all of the groups have completed their questions, I will model for them how to present the material to

the class. Each person will speak one person at time, and make sure to stay in character the entire time. Also, each student will be instructed to respect each other's argument, no matter how unrelated their argument may seem. After modeling these instructions, my students will act out these roles.

Closing

As a class we will summarize what we have learned about HIV/AIDS and how it relates to what we have been learning in the unit.

Homework

My students will be given a set of follow up questions to be answered and discussed in class the next day.

Future of Human/Virus Evolution Socratic Seminar

Objective:

+Respond verbally to open-ended questions +Exhibit and hone active listening skills +Hypothesize about the future evolution of viruses and humans

Anticipatory Set

Students will form two concentric circles with the desks in my room (one circle inside the other). It will be explained to the class that Socratic Seminars are question-driven discussions, named after the great philosopher, Socrates, who used questions to teach his students. In these discussions people don't talk over one another; they listen to each other's comments respectfully; they don't attack anyone's opinions and they agree to disagree.

Direct Instruction

I will instruct the students to split into two groups. Group A should sit in the inner circle and Group B should sit in the outer circle. I will then assign each person in Group B to a person in Group A. The Group B students should sit across from their partners in Group A so that they can keep track of their partners' comments and responses. At the end of the seminar the Group B students will give their partners feedback and constructive criticism about their participation in the discussion.

Modeling

During this part of the activity, I will model for the students all of the following steps. I will first pass out at least three strips of paper to each Group A person, and instruct them to write their names on each slip. When any student wants to make a comment, he or she must drop a slip of paper on the floor inside the circle. In order to get full credit for this activity, each person must use all of his or her slips. I will next explain that I am a silent facilitator: students should not look to me for justification or a change of direction for the discussion. They are responsible for answering each of the questions, and they may not move on to a new question if the one at hand hasn't been thoroughly addressed.

Guided Practice

I will then walk them through the following stage of the activity and pass out a list of open-ended questions

that refer to the text. It will be explained that only the people in Group A are allowed to speak during the discussion. Everyone in Group B must remain silent during the discussion

Independent Practice

My students will then be given a specific amount of time for the discussion and utilize that time to answer all of the questions that the students have.

Closing

When the discussion is over, Group B people will give constructive feedback to their Group A partners. Afterwards, I will give overall feedback to the whole group. The next time they participate in a seminar, Group B people will go into the inner circle.

Homework

They will be given a reflection handout to summarize what they've learned during the seminar. The reflection will be discussed the next day in class

Comic Book Project

Objectives:

- +Identify appropriate landscapes, characters, and props that relate to the events and characters they learned about in the unit.
- +Interact with classmates to give and receive feedback.

Anticipatory Set

The project will take about a week to complete. Therefore, I will only explain the first day of this activity. I will begin by introducing the writing activity, sharing the planning sheet, rubric, and sample graphic novels and comic books with the class. They will then identify what makes each example unique and explain how the examples benefit from their differences.

Direct Instruction

At this point, I will share the example graphic novels and comic books with students and explain the assignment, pointing out each of the parts that are included. I will then lead students through a discussion of the key elements for each part.

Guided Practice

Sample discussion questions will be given to the students to assist with this part of the activity. I walk them through examples of how to answer the questions. Questions may include the following: What are the important characteristics of a caption? What do the words in the captions tell you about the scene depicted? How are the characters (Humans and Viruses) connected in the story? Do the scenes reflect the themes of the story? What kind of dialogue bubble makes sense for the interaction? What connects one scene to the next in the comic strip?

Modeling

Once I'm satisfied that students understand the assignment, I demonstrate the Comic Creator student interactive and discuss its relationship to the Comic Strip Planning Sheet. I will make sure to cycle through the options for characters and dialogue bubbles to show students the range of options available.

Independent Practice

I will have students begin work with the Comic Strip Planning Sheet to plan their human/virus war stories. Students can work individually or in groups on this project.

Closing

Before class ends I will encourage students to interact with one another, to share and receive feedback on their plans for comic books. It will be explained to them the benefit of peer feedback since these comics will be shared in the class as well as in the library.

Homework

Students can continue working on the project for homework if desired.

Appendices

Implementing District Standards

3.1.B.B1.

Explain that the information passed from parents to offspring is transmitted by means of genes which are coded in DNA molecules. Explain the basic process of DNA replication. Describe the basic processes of transcription and translation. Explain how crossing over, jumping genes, and deletion and duplication of genes results in genetic variation. Explain how mutation can alter genetic information and the possible consequences on resultant cells.

3.1.B.B3.

Describe the basic structure of DNA, including the role of hydrogen bonding. Explain how the process of DNA replication results in the transmission and conservation of the genetic code. Describe how transcription and translation result in gene expression. Differentiate among the end products of replication, transcription, and translation. Cite evidence to support that the genetic code is universal.

3.1.B.C1.

Describe species as reproductively distinct groups of organisms. Analyze the role that geographic isolation can play in speciation. Explain how evolution through natural selection can result in changes in biodiversity through the increase or decrease of genetic diversity within a population. Describe how the degree of kinship

between species can be inferred from the similarity in their DNA sequences.

3.1.B.C2.

Describe the theory suggesting that life on Earth arose as a single, primitive prokaryote about 4 billion years ago and that for the next 2 billion years, a huge diversity of single-celled organisms evolved.

Analyze how increasingly complex, multicellular organisms evolved once cells with nuclei developed.

Describe how mutations in sex cells may be passed on to successive generations and that the resulting

Phenotype may help, harm, or have little or no effect on the offspring's success in its environment. Describe the relationship between environmental changes and changes in the gene pool of a population.

3.1.B.C3.

CONSTANCY AND CHANGE. Compare and contrast various theories of evolution. Interpret data from fossil records, anatomy and physiology, and DNA studies relevant to the theory of evolution.

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