YALE NATIONAL INITIATIVE
to strengthen teaching in public schools®

Curriculum Units by Fellows of the National Initiative
2014 Volume VI: Microbes Rule!

Making connections in science: viruses and the immune system

Curriculum Unit 14.06.07, published September 2014
by Kathleen Tysiak

Introduction

This unit is designed for an AP Biology course composed of junior and senior level students at George Westinghouse College Prep, a selective enrollment high school in Chicago's Garfield Park neighborhood. The course meets once a week for 50-minute class periods. GWCP is the first high school in Chicago Public Schools to offer a dual enrollment opportunity. Students can be accepted into the school by applying through the selective enrollment route, or by applying to one of the College to Careers programs including: Broadcast and Journalism, IT/Oracle, Medical, or Business. GWCP reopened its doors as a selective enrollment school in 2009, adding a class each year and graduating its first group of seniors in 2013. The school draws students from all over the city, representing almost 300 elementary schools and, therefore, serves students from a variety of education backgrounds. [1] It is not uncommon for students, even in an AP course, to have drastically different background knowledge and skill levels. The demographics represented at GWCP includes some diversity with approximately 64% of students African American, 28% of students Hispanic, 4% of students Asian, 2% of students White, and 1% of students multiracial or multiethnic. [2] 81% of students at Westinghouse qualify for free or reduced lunch. Additionally, GWCP is dedicated to preparing students for college, careers, and beyond by exposing every student to a rigorous curriculum and involving them in skills based learning. We hope to remain a school that is accessible to students in the community and view education as a strong platform for social change.

While Westinghouse has become a well-known school in the district, we still face many of the challenges that are seen at most urban, public schools. Budgetary cuts and community struggles result in negative impacts on student learning. As a result, many students experience deficits in science education in elementary school and feel those deficits follow them through their careers in secondary education. The students feel particularly challenged because science requires the integration of literacy and math while incorporating a specific subset of critical thinking skills often termed "scientific thinking skills." On our state achievement exam assessed in April of junior year, science is the only subject area in which GWCP students do not exceed both the state and district percentages of students meeting and exceeding standards. In both 2012 and 2013, 46% of students met or exceeded standards on the science portion of the exam. Based on the ACT benchmarks, only 25% of GWCP students were ready for college coursework in science. These trends are reinforced when students find it acceptable to justify these results by saying they are simply not "science people."

One way that GWCP has begun to increase student achievement is to increase exposure to AP level courses. Since starting AP Biology in the 2012-2013 school year, I have instructed between 40 and 60 students each year. I had the fortune of beginning to teach the course during its first year after the College Board revamped the curriculum to decrease content and increase science practices and mathematical analysis. Each year, I take the opportunity to reflect on lessons and make changes that I know will be best for my students. Still, I continue to find it a challenge to keep students engaged while helping them master the immense amount of content at the required skill level for an AP Biology course.

Rationale & Objectives

The purpose of this unit is to foster the development of literacy, scientific/critical thinking, argumentative, and discussion skills while engaging students in highly relevant content. Even when students are interested in concepts in Biology, the content can easily become overwhelming and inaccessible when vocabulary and skills requirements come into play. By immersing students in the complexities involved in HIV vaccine development, I intend to help students create foundations of understanding of viruses, particularly HIV, the immune system, and vaccines. The way the content will be delivered will also help students form connections to the bigger ideas that drive all concepts in Biology and that are emphasized by the AP Biology curriculum. To help students make these connections, we will address the following essential questions:

- How does our body protect us from disease?
- Why do viruses make us sick and why, if viruses are all around us, are we not sick all the time?
- How do the mammalian immune system and the structure of viruses explain vaccines?
- Why is there no vaccine for HIV?
- What should be the next steps for tackling the AIDS epidemic?
- What ethical considerations must be taken into account when conducting scientific research and making scientific advancements?
- How will the "host-pathogen arms race" impact our future as a species?

Background

Immunity

Most organisms exhibit some version of an immune system that protects against harmful infections. Even unicellular organisms have a wide array of defenses against pathogens such as bacteria and viruses. In fact, many of these same defenses have been conserved or utilized in more recently evolved multicellular organisms [3] . Most vertebrates, including humans, have two classifications of immune responses to protect against harmful invaders and internal sources of damage, such as cancer. These two types of responses are innate (nonspecific) immunity, and adaptive (specific) immunity.

Innate/Nonspecific Immunity

Innate immunity includes all factors that try to keep out invaders and which attack pathogens or harmful objects regardless of their identity. In humans, this type of immunity is the body's immediate defense against harmful substances, including its own cells whose mutations may cause harm to the organism as a whole. The body's preliminary innate defenses include the skin, mucosal membranes, hairs, and cilia. Even bacteria found

in or on the body can reduce the potential of infection by other, harmful bacteria by outcompeting these bacteria for nutrients and binding sites. These mechanisms work to keep pathogens from ever entering the body or by trapping and "sweeping" them out before they can enter internal structures. Once a pathogen enters the body, or if harmful mutations form, the body has a variety of secondary defenses and mechanisms of protection. Many general feelings of malaise and sickness that people experience are results of the body's immune response. The achy feeling is actually the body's blood vessels expanding to increase the migration of white blood cells to the site of infection. Elevated body temperature, or fever, may create inhospitable environments for these pathogens and/or may improve the immune system's efficiency—the purpose is debated. [4] A variety of white blood cells, can work to phagocytize, or engulf, pathogens and degrade them. The most commonly referenced phagocyte is a macrophage. These white blood cells can also activate other white blood cells to help fight infection and can work as antigen presenting cells, which ties to adaptive/specific immunity, described below. Other white blood cells, known as natural killer cells, look for basic markers on cells, called Major Histocompatibility Complexes, or MHCs, that identify cells in the body as "self." Cells that do not have the form of MHC's found on that individual's cells are recognized as invaders or damaged and are stimulated to undergo programmed cell death; apoptosis. Since none of these interactions are specific to the type of pathogen infecting the body, they are all part of the nonspecific, or innate immune response. Innate responses, as a result, do not change as a result of a pathogen infecting the body more than once [5] .

Adaptive (Acquired)/Specific Immunity

Soon after infection by a pathogen, an adaptive response begins to occur. Cells involved in adaptive immunity do more than recognize invaders as "non-self," they recognize, and respond to specific pathogens. This type of immunity is especially beneficial in its ability to "remember" specific pathogens and build a quicker response after a secondary infection. In fact, it is this natural benefit of adaptive immunity that has been exploited by scientists in the development of vaccines, which allow people to form immunity against pathogens before being infected. Vaccines will be discussed in more detail below. The cells involved in adaptive immunity are divided into two classes: humoral and cell-activated.

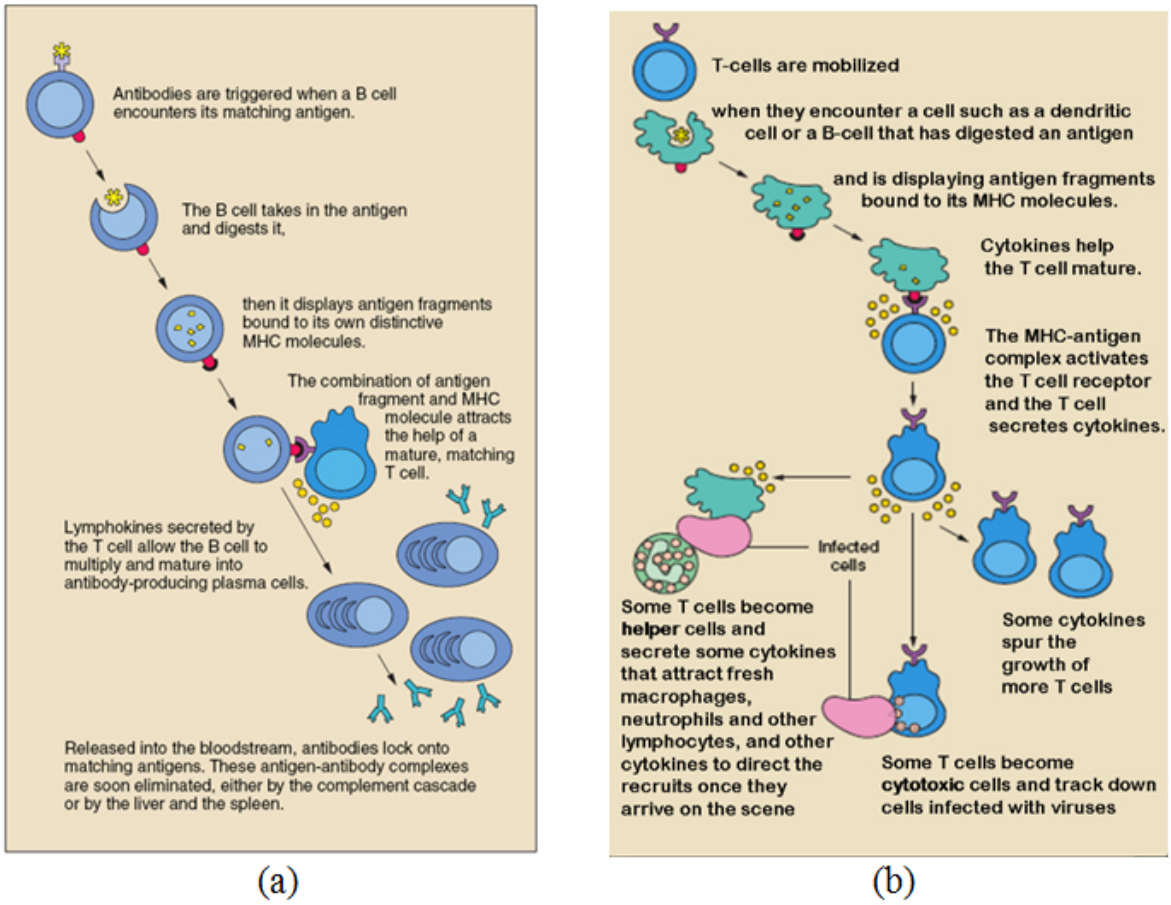

Figure 1: An illustration of the major types of cells involved in (a) humoral immunity and (b) cell-mediated immunity.
Courtesy: Template drawing and caption from "The Immune System" Wikimedia Commons (Public Domain)

Humoral

Humoral immunity involves a specific type of lymphocytic white blood cell, called a B cell. B cells contain proteins on their outer membrane, called antigen receptors that recognize a specific antigen (invading pathogen, or mutant cell). In B cells, antigen receptors can recognize a variety of types of molecules from invading or mutated cells including surface proteins, polysaccharides, or even lipids. The antigens recognized can either be presented by an antigen-presenting cell, discussed later, or by a free-floating pathogen. When an antigen from one of these cells binds to the antigen receptor of a B cell, it, in effect, activates the cell and causes it to divide. Signals from T cells, another type of lymphocyte, cause these B cells to differentiate into either plasma B cells or memory B cells. [6] Plasma B cells are able to release antibodies, which, like the antigen receptors, recognize these specific antigens. Antibodies bind to the antigens and can neutralize the pathogen, mark them to be phagocytized by a macrophage, or signal to Natural Killer cells to stimulate apoptosis in this cell. [7] Most of these plasma cells undergo apoptosis once the cause of infection has passed. Memory B cells, however, remain in the body. Since these B cells are already developed against a specific antigen, upon secondary infection by the same pathogen, the body will be able to build an immune response much faster. Essentially, the body is remembering the pathogen so that it can remove the problem before the individual

feels the effects of infection. It is important to remember that this immune memory is dependent upon the specificity of the antigen. Therefore, the strain of the pathogen must be similar enough to be recognized by the antigen receptors in order for a secondary immune response to be activated.

Cell-mediated response

The other type of adaptive immunity, known as cell-mediated response, involves another type of lymphocyte, called a T cell. Like B cells, T cells have antigen receptors. These receptors, however, are only able to recognize antigens that have been presented by an antigen-presenting cell, such as a macrophage. For example, in nonspecific immunity, a macrophage may phagocytize a bacterium. This macrophage will use enzymes to degrade the bacterium and will present parts of the degraded antigens on Major Histocompatibility Complexes (MHCs). There are two main types of T cells: Helper T cells (T_H cells) and cytotoxic T cells (CTL cells). When the antigen receptor of a T_H cell binds to the antigen presented by the MHC of a phagocytic cell, these T_H cells are activated and stimulated to proliferate (expand in number). T_H cells aid in the immune response by secreting chemical signals that activate other T cells, B cells, and other cells that play a role in the immune response. The other major types of T cells, CTL cells, are also activated when their antigen receptors bind to an antigen presented by an MHC. The type of MHC required for this process, however, is only found on certain types of cells. This binding will activate the CTL cells and cause them to multiply. The activated CTL cells may, for example, recognize and bind to an antigen presented by an MHC on a cell that has been infected by a virus. The CTL cell is able to perforate the infected cell and cause it to undergo apoptosis. Whereas helper T cells activate other types of cells, cytotoxic T cells are directly responsible for destroying cells that are infected with pathogens. In both cases, most T cells undergo apoptosis once the infection has cleared. Some, like with B cells, remain in the body as memory cells to generate a more efficient response in the instance of infection by the same pathogen at a later time. [8]

Vaccines

In today's society, it is common to manipulate the immune system to keep people from ever getting sick by a disease. This is done through the use of vaccines. By exposing the body to an antigen, usually one that has been modified so that it no longer causes disease, the body can develop an immune response. If the body is then re-exposed to the actual pathogen, their body will already have memory cells for that antigen and will be able to quickly build an immune response "before it can inflict damage that results in symptomatic illness or death." [9] The first attempted control of a disease with vaccine, and the only disease ever eradicated through the use of vaccine, is smallpox. This vaccine is usually credited to Edward Jenner, though more recently he has been accredited with the research and publication of results that led to widespread vaccination.

In actuality, it is believed that variolation, a form of inoculation in which fluid from the smallpox-virus pustule of an infected individual was put beneath the skin of an uninfected individual, was practiced in Africa, India, and China in ancient times. The small exposure often reduced the likelihood of infection by smallpox virus from the environment. [10] It is no wonder that humans had tried to control the disease as smallpox had been wreaking havoc on the human species since sometime around 10,000BC. [11] In addition to causing the iconic pustules or "pox," infection by this virus led to disfigurement, blindness and, commonly, death. Smallpox has single-handedly affected the history of humans. In the late 1800s, the mortality rate from smallpox in Berlin was 98%. In 18 th century Europe, roughly 400,000 people died of smallpox per year. Of the survivors, 1/3 went blind. Smallpox nearly wiped out native populations in the New World as a result of introduction by European explorers carrying the virus. During the Middle Ages, smallpox decimated populations and greatly

impacted civilizations. It may be linked to the fall of the Roman Empire and has even been discovered on mummified remains of Egyptian pharaohs. [12] Those that were lucky enough to survive a smallpox infection were immune for life. It was this observation that led to the spread of variolation to Europe. Though heavily influenced by social issues, over time variolation became a common practice in Europe and, eventually, in the New World. Though 2-3% of people died as a result of variolation, the mortality rate was much lower than the 14% of natural smallpox virus infection. [13]

After taking much interest in the subject, and having been variolated himself, in the late 1700s Edward Jenner observed that milkmaids who had been infected with cowpox, a nonfatal disease, also seemed to have immunity to smallpox. Having already been extensively trained as a physician, surgeon, and researcher, he conducted an experiment in 1796. In this experiment, he infected an 8-year-old child with cowpox virus and, two months later, infected him with the smallpox virus. The boy did not get sick. Jenner published his findings and conducted follow up surveys. Eventually, the practice of using this vaccination (named after cowpox, "*vaccinia*") became common practice and, after the World Health Organization launched a global vaccine campaign, smallpox was eradicated in 1977. [14] With more information about the mechanism behind why this vaccine works, we have since been able to create vaccines for numerous pathogens.

Viruses

Many of the pathogens that commonly cause disease in humans, including smallpox, are viruses. Though it has been a cause for debate, viruses are generally considered nonliving due to the fact that they do not metabolize or respond to stimuli. These particles are often incredibly small, roughly 10 to 400 nm in size [15] ; viruses are not made of cells and require the replication machinery of host cells to reproduce. Viruses are, however, able to evolve and replicate. In fact, most of the genetic diversity of life is found within the genomes of viruses. [16] Life cycles differ by virus, which is discussed in more detail below. These structures of genetic material and protein have a massive impact on the environment. Infecting plants, animals, and in the case of bacteriophages, bacteria, these viruses impact population dynamics, community stability, and even abiotic factors such as global climate and oxygen production. In fact, it has been calculated that "10 percent of all the photosynthesis on Earth is carried out with virus genes." [17]

Structure and Life Cycle

The structures of all viruses are the same in two ways: they contain an outer capsid, which is a structure made up of proteins, and they contain viral genetic material. Some viruses have envelopes inside their capsids while others do not, and the type of genetic material differs amongst viruses. [18] This size of viruses varies greatly, though the overwhelming majority of viruses are significantly smaller than bacteria. To provide perspective, about 1,000 viruses could be lined up along a grain of salt, in comparison to about 100 bacteria or ten skin cells. [19] The size of a virus does not correlate to the size of the host that it infects. In fact, one of the largest known viruses infects single-celled amoeba. [20] Viruses are grouped by the type of genetic material they contain (DNA or RNA, single or double stranded) and how the viral genome is replicated. [21]

Viruses may undergo one of two life cycles: lytic or lysogenic. A virus begins infection when a part of its capsid attaches to a receptor on the outer membrane of a host cell. Due to the specificity of binding, each virus is only able to enter specific host cells. After attachment, the genetic material of the virus enters the cell and uses the host cell's replication machinery to make additional copies of its genetic material and the proteins required to form new copies of viral structures. If the virus is in a lytic cycle, this happens immediately and the

virus erupts from the cell, causing lysis, or bursting of the host. Certain bacteriophages may also have a lysogenic life cycle, in which the viral DNA is inserted into the host DNA, remains dormant, and can be passed on through future generations. The period of dormancy is called latency and can vary in length. Eventually, reactivation can occur in which the viral DNA is copied, transcribed, translated, and new viral particles are assembled. This will result in the release of these viruses. [22] Animal viruses may also experience periods of latency in which viral DNA is inserted into the host genome and various lengths of dormancy occur. The exact mechanism of viral replication is particular to specific viruses and is linked to their type of genetic material. Retroviruses are of particular note because they use an enzyme called reverse transcriptase to turn their RNA into DNA. This DNA (referred to as cDNA) is then inserted into the host genome, which can then be used to make more viral RNA and proteins. It is also possible for the cDNA to be transcribed and translated without inserting into the host genome. Viral replication can occur so quickly that, upon entry of a cell, thousands of viruses can be synthesized within a day. [23] With latent infections, viral DNA can also remain in host genomes for prolonged periods, even so far as to be inherited by offspring. If mutations occur, these genes can remain in the genome permanently without the possibility of jumping back out of the host genome. In fact, approximately 8%, close to 100,000 fragments, of our own, human DNA is not human at all—but believed to be of viral origin. [24]

Evolution of Viruses and their Impact on Human Evolution

Based on the life cycle and genetic diversity of viruses, it should be of no surprise that viruses are known for their rapid evolution. This can be attributed to recombination, high mutation rates, and short life cycles. DNA viruses, in general, have the lowest mutation rates among viruses, though single stranded DNA viruses have been found to have mutation rates only slightly lower than some RNA viruses. [25] The mutation rate in double stranded viral DNA is similar to the mutation rate in host DNA, but, as one study suggests, may result in more mutations overall due to the number of times this viral DNA is copied during a cellular infection. This study estimated the mutation rates to be 10^{-8} -10^{-6} substitutions per nucleotide per cell infection. [26] RNA viruses, by comparison, lack molecular proofreading. The same study estimated that RNA viruses have mutation rates in the range of 10^{-6} -10^{-4} substitutions per nucleotide per cell infection. Retroviruses have even higher mutation rates because reverse transcriptase "operates close to the error catastrophe threshold, the level of critical-copying fidelity below which information can no longer be maintained." [27] The mutation rates of all RNA viruses tend to be much lower if they insert their genetic material into that of the host cell. [28]

In addition to mutations, viral genomes are able to recombine. In RNA viruses, for example, the RNA polymerase used to create more copies of viral RNA can switch the strands that it uses as a template. [29] Additionally, if a host cell is infected with more than one type of virus, the genomes of these viruses are able to recombine, resulting in a type of horizontal gene transfer between viruses. One study found that recombination rates were about 4% when a host cell was infected with two retroviruses. [30] High mutation rates, high recombination rates, and the speed at which viruses are replicated, all lead to the potential for rapid rates of evolution. These changes to viral genetic material can be deleterious, neutral, or positive. By increasing virulence or the ability for a virus to increase the survival time of its progeny, these viral mutations can be selected for, resulting in an overall improved fitness change of the viral population. These observations have also been used to explain why RNA viruses are less species specific and can more easily jump from one species to another, as is the case in zoonoses (animal acquired infections) and most emerging viruses. [31]

The rapid evolution of viruses has also had a major impact on the evolution of other organisms. The phenomenon of host organisms' need to keep up with ever-changing viruses has been described as a "host-

pathogen arms race." [32] It is hypothesized that humans and their ancestors have long been infected by DNA viruses, though these viruses likely had less of an impact on their evolution. This may also have been true of RNA viruses that have latent life cycles and, thus, are more stable. RNA viruses with high rates of evolution, on the other hand, more likely had an impact on human evolution. These viruses may have become more prominent when humans began domesticating animals and attracting disease-carrying rodents to their more permanent homes, allowing the viruses to more easily jump into humans. It is possible that some species of hominids were more susceptible to certain types of viruses, acting as "agents of selection." [33] The pressure of viruses may have encouraged genetic diversity in the human genome, especially when it comes to MHCs. It has even been suggested that in an earlier common ancestor, the "need for genetic diversity…contributed to the evolution of sexual reproduction." [34] The selective power of viruses on host genomes suggests the possibility of a type of coevolution between parasite and host. Retroviruses and DNA viruses that are able to insert their genomes into host DNA likely had a more direct role in changing the human genome, as can be seen with current human genes that have been identified as having originated as viral genes. The ability of humans and other placental mammals to develop a placenta is linked to an ancient virus-derived gene similar to that found in human endogenous retroviruses. [35] With the new evidence that viruses may have had a large impact on human evolution and their hominid relatives, it is clear that there is still much to learn about viruses.

HIV

HIV Infection

One virus that is of particular human disease interest is HIV. HIV, or human immunodeficiency virus, is the virus that causes Acquired Immunodeficiency Syndrome, AIDS. HIV continues to pose a major threat to humans. Worldwide, according to the CDC, about 35.3 million people are living with HIV infection, with 2.3 million new cases occurring each year. In 2012, an estimated 1.6 million individuals died as a result of AIDS. In the United States, approximately 1.1 million people are infected with HIV, 16% of whom are unaware of their status. [36] In Washington D.C. (as of 2009), 3% of the population is infected with HIV. This rate is twice as high for African American males. [37] In 2011, Chicago reported an HIV prevalence rate that was 3 times greater than the national average, with HIV-infection and AIDS-diagnosis rates that were twice the national averages. [38]

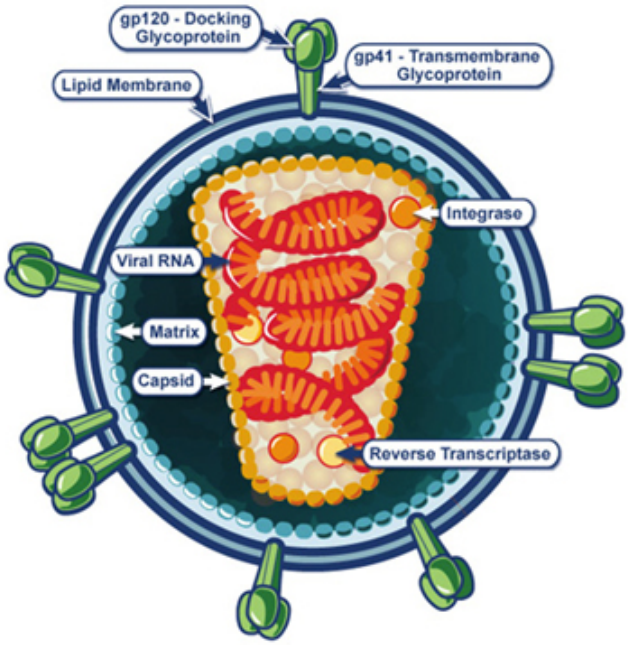

Figure 2: An illustration of the structure of an HIV virus including the RNA genetic material, capsid, envelope, and membrane proteins.
Courtesy: National Institute of Allergy and Infectious Diseases

While there is no cure for AIDS, the impact of HIV on the human population has promoted extensive research of HIV's structure, life cycle, and infection mechanisms. HIV is a single stranded RNA (ssRNA) virus that has two copies of its viral genome. These viral RNA molecules are non-covalently linked at their 5' end. [39] The virus itself is composed of an envelope made up of a lipid bilayer with viral proteins. Beneath this envelope is the capsid, within which is the viral RNA and reverse transcriptase enzyme. When HIV encounters a CD4+ T cell (a type of helper T cell), the virus attaches to CD4 receptors and co-receptors (usually CCR5 or CXCR4). This attachment allows the viral capsid to enter the T cell. Reverse transcriptase uses the viral RNA to create a DNA strand within this capsid. This viral DNA is inserted into the host genome and, eventually, used to make more copies of the viral RNA and viral proteins. This allows the virus to escape the cell and infect more CD4+ T cells. [40] AIDS is established once the number of surviving CD4+ T cells falls below a certain level, compromising the immune system of the individual.

There are two main types of HIV: HIV-1 and the less virulent form, HIV-2. It has been hypothesized that HIV-2 emerged as a result of a bite to a human from a mangabey monkey, which carries a similar lentivirus. [41] HIV-1 likely jumped into the human population from chimpanzees when they were killed for meat by hunters. This did not pose a problem to the global population until these hunters began entering cities and the virus spread between humans. HIV-1 is estimated to have been in the human population since roughly 1933, though it wasn't recognized until 1983. [42] HIV-1 is further split into groups: M (main), O (other), and N (non-M; non-O), each of which is predicted to have independent origins of transmission. [43] While Types O and N are only found in Africa, Group M is found everywhere and has been split into subtypes A-D, F-H, J, and K. Sub-Saharan Africa has the greatest diversity of HIV-1 representing subtypes A, C, D, F, G, H, J, K. 50% of the HIV infections worldwide are subtype C, though Subtype B is the most highly represented in the Americas, Western Europe, and Oceana. [44]

Current HIV Treatment

Current treatment for HIV includes the use of a cocktail of drugs referred to as Highly Active Anti-Retroviral Therapy, or HAART. These drugs work by inhibiting reverse transcriptase, keeping viruses from replicating, and by stopping HIV viruses from entering CD4+ T cells in the first place. In recent years, these drugs have been fairly successful in allowing people to live mostly normal lives. Still, these treatments are extremely expensive, and, as such, "has meant that most people with HIV—living in the poorest countries—cannot afford a treatment that might give them extra years or even decades of life." [45] Still, these drugs have negative side effects that can be harmful to humans after years of treatment and encourage the proliferation of viruses that are unaffected by these drugs. [46] This becomes especially concerning when it is recognized that 26% of new HIV infections in the United States occur in people ages 13-24. [47] Dr. Anthony Fauci, the head of the National Institute of Allergy and Infectious Disease, has continued to conclude that, "the development of an HIV vaccine must remain at the top of the global health research agenda." [48]

The Struggle to Develop a Vaccine

Though HIV vaccines have been researched for over 20 years, no successful vaccine has been developed and released to the public. Though some vaccines have made it to trial stages, none have been approved for public use. In 2008, a vaccine developed by Merck went through human trials. These trials were shut down after it was found that the vaccine was actually making people more susceptible to HIV infection rather than less. [49] There are a variety of reasons that scientists have had a hard time developing a vaccine against HIV. Most classical vaccines mimic the response some individuals are able to naturally mount against the infection of that pathogen, as is exemplified with the smallpox vaccine. This concept is called "proof of concept." [50] While some individuals are able to survive for longer periods of time with an HIV infection before succumbing to AIDS, no one has ever been cured of an HIV infection. Scientists are faced with the challenge of creating a vaccine that "produces a protective immune response that is superior to that elicited by natural infection." [51] The elusiveness of HIV can be attributed to its ability to establish latency, its high mutation rate, its high likelihood of recombination, its ability to evade immune system cells, and its direct attack on the immune system itself.

As previously stated, HIV is a retrovirus and as such, has a high mutation rate. One study calculated HIV's mutation rate to be $4x10^{-5}$ mutations per target base pairs per replication cycle in T cells. [52] A different study found that homologous recombination is also frequent in HIV-1 viruses, occurring $2.4x10^{-4}$ times per base pair per replication cycle. This can take place when the reverse transcriptase switches the template strands, known as "copy choice." [53] Increase in HIV diversity through recombination would be particularly high in cases that a host cell is infected by more than one strain of HIV.

These rapid changes in HIV's genome contribute to its ability to evolve quickly. In a study conducted by Song, et al., the change in viral genotypes was analyzed in vivo. Within 2 weeks, the original strain of HIV made up less than 10% of the HIV population. Of the other genotypes, 2 main mutations were identified. One mutation allowed HIV viruses to escape cytotoxic T lymphocyte (CTL) detection. Mutations such as these are referred to as CTL escape mutations. These mutations have previously been found to have negative affects on viral replication. A different mutation was categorized as a reversion mutation. The majority of viruses analyzed had both of these mutations within 14 days. 592 days after initial screening, 100% of the cells had both mutations. [54] Additionally, these viruses were shown to not suffer reduced replicative fitness. [55] This information suggests that the selective pressure of CTL cells reduced other HIV strains, allowing the mutated HIV to proliferate and increase their capacity to evade the immune system. Similarly, in the case that scientists were able to develop a vaccine, the high mutation and recombination rates of HIV would likely make

these vaccines ineffective. The evolution of HIV has also allowed it to evade the immune system by changing the carbohydrates and proteins the immune system would use to identify HIV. [56] At the same time, HIV quickly establishes latency in host cells, "likely within days." [57] This dormant period allows the viruses to hide from the immune system, remaining undetectable until they reactivate and spread throughout the body. It is as if, as the body wages war against the viruses it can see, HIV is building an unseen army, ready to be deployed at any time.

Some positive discoveries have been based around conserved sequences of one of HIV's surface proteins, gp120. This protein allows HIV to enter host cells and, therefore, cannot change much or HIV will lack its invasion abilities. Scientists have begun to find antibodies that are capable of neutralizing HIV and recognize this conserved sequence. One such antibody, announced in 2010 called VRC01, was found to neutralize 90% of common HIV-1 strains. [58] Still, administering antibodies is currently a method of treatment rather than prevention. It will be a challenge for scientists to determine how, if these are used to create a vaccine, these antibodies could be induced in the majority of people. [59] Other scientists have begun to investigate the population of people in Europe who are naturally immune to HIV infection due to a mutation in their CCR5 co-receptor. In one study, an individual underwent successful stem cell transplant with blood stem cells that were homozygous for the mutated genes. The results reported that after 20 months, HIV-1 could not be detected in the individual, indicating control of the HIV infection. Still, scientists are concerned with mutated strains of HIV-1 known to bind to a different co-receptor. Individuals with the CCR5 mutation would not be immune to these strains of HIV. [60] Additionally, the challenging and invasive stem cell transplants present as a treatment, rather than preventative, option. As scientists continue to explore preventative options, Dr. Fauci suggests that, perhaps, scientists need to think unconventionally and investigate manipulating the innate immune response in a way to "better protect the body at the most frequent points of entry of the virus" such as the mucosal membranes. [61] As the search for a preventative vaccine continues, it is clear that rapid evolution of the virus continues to elude both the human body and scientists.

Strategies and Activities

The strategies presented are designed to help students practice using models and interact with text to access the extensive amount of information required by the AP Biology curriculum. My goal is that by delivering lessons in this manner, students will not only build these skills, but will interact with the content in a way that will help cultivate the curiosity that will propel them through the unit. In doing so, students will look to use the concepts they are learning to make connections with the big picture ideas and ask the questions that are relevant in society today.

Activity One: Introduction and Immune System

The unit will begin with students activating prior knowledge by looking at a Wordle (see Appendix B) and self-assessing which words they are strongly familiar, somewhat familiar, and unfamiliar. In addition to students being able to access prior knowledge and identify concepts that may prove to be more of a challenge, this will give students the opportunity to preview vocabulary for the unit. Students should also predict the important topics and concepts that will be pertinent to the unit.

Once students have previewed the unit, they should move into the immune system. Since the end goal is for students to make connections between the coevolution of pathogens and their hosts, as well as understanding why HIV vaccines have been so evasive to the scientific community, they will need to have an underlying comprehension of how our immune systems work to protect us against disease. It is likely that, in my classes, some students will have heard the word innate before. After defining the term as a class, it will be applied to immunity and students will brainstorm parts in the human body that make up the innate immune system. I predict that, as a class, students will be able to come up with things like the skin, mucosal membranes, and cilia. It is also likely that they will need to be introduced to terms like macrophages, MHCs, and the immune response. A variety of animations and videos are available online to help students visualize these processes. After being introduced to these concepts, students will be asked to create their own models or outlines of the innate immune system and immune response.

A similar protocol will be used to introduce the idea of acquired immunity. It is pertinent that students have a strong understanding of the humoral acquired immunity since it is the T helper cells that are directly invaded by HIV. To foster student's understanding of immunity, students will complete a POGIL ™ activity from the *POGIL ™ : Activities for AP* Biology*. This resource is available through Flinn Scientific and presents models to students for analysis. The immunity activity uses models to introduce both cell-mediated and humoral acquired immunity. The process is designed so that students work in groups to investigate models. At important intersections, we stop as a class to discuss the material. Particularly important is investigating the questions that emphasize key ideas or higher-level questions. Even with straightforward questions, there are times when the phrasing and vocabulary involved make them difficult for students to access. One protocol we have used in class is to ask students to write out all sub-questions required to answer the question presented. This requires students to create their own scaffolding and build the metacognitive skills required to break down questions and, thus, answer higher-level questions. Upon discussing humoral immunity, I will ask the students the follow up question: "What is the significance of antibody specificity?" It is likely that students will struggle with this question and will need to use the same protocol to decode the question. Questions similar to this one will also help students contrast innate and acquired immunity, which can also be referred to as nonspecific and specific. We will not complete the extension questions of this activity since these concepts will be introduced through the next activity. Upon completion of the POGIL ™ , students will create a graphic organizer with vocabulary and phrases to help them organize important information. The students should be able to complete the graphic organizer outside of class, but it is recommended that they brainstorm with peers the important topics and contents that should be included.

These activities should take approximately three days but students should have a sound understanding of the processes of innate and acquired immunity. They should be able to contrast the types of immunity and differentiate between cell-mediated and humoral acquired immunity. Students should be able to use vocabulary, such as cell types and their roles, while explaining these processes and identifying the significance of pathogen specificity in acquired immunity. Finally, students should relate pathogen specificity and immune memory to articulate why secondary infections result in rapid and heightened immune responses.

Activity Two: Viruses and their Evolutionary Role

After learning about the immune system, students will be in a place to understand how vaccines manipulate the immune system into protecting a person against a particular pathogen. Since smallpox and HIV will be used as a paradigm to teach the history and functionality of vaccines, I intend to first help students develop stronger understandings of viruses. The first part of this activity will involve students identifying similarities

and differences between various viruses that are illustrated in their textbook. The viruses included are: Adenovirus, a bacteriophage, Tobacco Mosaic Virus, and Influenza Virus. These viruses are an excellent sample because they show variety in genetic material, presence of an envelope, viral structure, and include bacteriophages that infect bacteria. By comparing these models, students should be able to identify that viruses all have a genetic material and capsid. This, in general, defines viruses. Viruses are, however, able to infect different cell types, contain different types of genetic material, and can have very different structures, including the presence of a viral envelope. Students will have previously been asked to read the forward and introduction from Carl Zimmer's *A Planet of Viruses.* Students will be asked what stuck out to them about the reading and how it relates to what we are studying. After a short discussion, we will also look at the images found in the textbook that illustrate the viral life cycle. Students will be asked to write a description of viral life cycles with a partner, being sure to compare and contrast the lytic and lysogenic life cycles of viruses. As part of a whole class discussion, I will ask students which type of a life cycle is more destructive. I predict that most students will identify the lytic life cycle as more destructive. As a follow up question, I will also ask students how the lysogenic cycle of a virus, or any latent stage of an animal virus, could potentially be more destructive to a species? My goal in this exercise is to get students thinking about the infectious aspect of viruses and how latent phases of viruses can actually increase the spread of an infectious disease.

I also want students to have an opportunity to learn more about a variety of viruses while gaining deeper knowledge about the classifications and specifics of viral structure and life cycles. To cultivate this curiosity and foster discovery, I will assign all students to read the Endogenous Retroviruses chapter of *A Planet of Viruses* while also allowing them to choose an additional chapter from a selection about other viruses including: Rhinovirus ("The Uncommon Cold"), Influenza ("Looking Down from the Stars"), Papillomavirus ("Rabbits with Horns"), Bacteriophages ("The Enemy of our Enemy"), marine phages ("Oceans of Viruses"), West Nile ("Becoming an American"), or SARS and Ebola ("Predicting the Next Plague"). In small groups, students will have to share the type of virus they read about, how it connected to what we've been learning, any hints as to what type of life cycle it has, and any additional information that was of interest. They will also have to discuss why I thought it was important that all students read about Endogenous Retroviruses and identify the main ideas of the chapter. My goal is that students will practice using vocabulary to discuss their reading while also practicing comprehension skills and making connections to the content. Not only will this help facilitate literacy skills, but it will introduce them to a variety of fascinating information and imagery that should propel them through some of the more conceptual topics. Another goal of integrating these readings is that they show the versatility of viruses and begin to touch upon their role in our history as a species. It will also get students thinking about how these viruses will also play a role in our future. Upon completing the partner discussions, we will do a share out with the entire class to verify that all students are on the same page about viruses so far.

The next part of this activity is centered around an additional reading. Students will read pages 15-18 and 31-32 of the article "Role of Viruses on Human Evolution" by Linda M. Van Blerkom. These reading sections include much of the Introduction and Discussion sections of the text. While reading, students will be asked to identify: clarifying questions, main ideas, and points of interest. Once groups have concluded compiling their information, they will be asked to share with one another on posters through the room. This will help students visualize information and guide a group discussion. Students should also be able to make connections to the chapter on Endogenous Retroviruses that they all read from *A Planet of Viruses* in addition to information from their selected chapter to help them explain the role that viruses and humans play in the evolution of the other. As a facilitator in the classroom, I will be sure to make sure that the discussion defines the concept "pathogen-host arms race" as is referenced in both readings. Upon completion of the activity, students should be able to explain what all viruses have in common while also indicating the differences that can be found

within the objects. Within this three-day lesson cycle, students should be able to articulate the life cycles of viruses, including lytic and lysogenic stages, and should indicate how these life cycles can impact the pathogen. They should also be able to articulate the impact of latency on the ability of a virus to "survive." Finally, students should be able to explain how the relationship between pathogen and host results in a continuous evolution of each.

Activity Three: Vaccines

Once students have had an opportunity to investigate viruses in more detail, they are ready to go back and make the connection between the pathogen and immune system. The development and mechanism of vaccines is a great way to tie these concepts together. As the first vaccine and the only virus to be eradicated from the planet, smallpox is an excellent paradigm through which to teach students vaccines. I intend to begin this discussion with having half of my class read "Edward Jenner and the history of smallpox and vaccination" by Stefan Riedal and the other half read the chapter on smallpox, "The Long Goodbye," from *A Planet of Viruses.* These articles look at the history of smallpox and the creation of vaccines from two different lenses, while still emphasizing the process of vaccine development and the role they have played in our history.

To facilitate a discussion, I intend to use a fishbowl protocol that has been tweaked by faculty at my school to integrate technology and increase engagement. As per a normal fishbowl activity, half of the class will begin in the inner circle, with the other half of the class seated in a circle surrounding their peers. The "inner circle," however, will actually have two tables that face each other. One table will include students that read the article, while the other table will seat students that read the chapter. These students will be asked to share with each other the main ideas and supporting details that were presented in each of their readings. They may also share concepts that students felt were important or interesting. In fact, each article contains its own commentary on social or ethical interests, which will likely draw in students during reading. I expect that these commentaries will also help liven discussion. The students on the outside of this circle, will be able to use computers or their cell phones to access a program or website, such as Todays Meet © at www.todaysmeet.com. This website allows you to create a room for your class in which students are able to enter their own name and submit comments in real time. By connecting a computer displaying the site to a projector, the students on the outer circle will be able to silently participate in the discussion by adding their own comments or reactions to the discussion. At this time in the school year, students will have already participated in enough discussions that they will know the classroom norms. Still, we will review them prior to beginning the discussion. Additionally, students will be reminded how they get credit for participation in a discussion. This will include participating at least once in which they directly reference a page or quote in the text and explain the significance of that selection. They will also have to react to another student's comment and will receive credit for following norms.

Once students have had time to participate, I will request that the inner and outer circles exchange places. The inner circle will then be expected to discuss the crosscutting concepts that they heard based on the discussion of the previous group. They will also be asked to identify implications of the content discussed from the readings. Again, students in the outer circle will be able to participate in this discussion by adding their thoughts or reactions to Todays Meet © , which will be projected on the board. This type of facilitation enables students to interact with each other, even if they are not all part of the inner circle. In the case that a student has high anxiety in participating in front of the class, students can also get credit for their Todays Meet © contributions and/or by posting a reflection and reaction to the class webpage. Upon completion of this discussion, we will end the class by connecting this information to how vaccines work. Students will be asked to answer the question "How do the mammalian immune system and the structure of viruses explain the use

of vaccines?" Students may need time to talk through their thoughts with a partner before settling on an agreement as a large class. Optimally, this activity will take two days to complete with the intended outcome being that students are able to answer the aforementioned question by linking the structure of viruses and the mechanisms of mammalian immune systems.

Activity Four: Understanding HIV

Before students will be ready to have academic conversations about the struggle to develop vaccines for HIV and theorize what can be done to solve this problem, they need to have a strong background knowledge on the structure and life cycle of HIV, as well as why it is such an area for concern of the human species. Students will begin their introduction by reading the chapter on HIV in *A Planet of Viruses*, entitled "The Young Scourge." This chapter provides a very basic overview of the virus, the impact it has had on the human population around the world, its origin, and a brief description of how it infects cells. After students read the chapter, they will have a chance to share their reflection of the reading, but this will be brief.

They will then spend approximately three days on an activity that I will modify from the National Center for Case Study Teaching in Science created at the University of Buffalo. This particular activity, entitled "Resistance is Futile—Or is it?: The Immunity System and HIV Infection," is written by Annie Prud'homme-Genereux from Quest University in Canada and is available online (see Appendix B). In Part I, I do not intend to give my students the diagram of HIV infection but, instead, will change question 1c to require students to diagram this process on their own. Additionally, I will ask my students why the illustrators chose to use a key to represent gp120. This will help students develop a stronger understanding of the role of this protein but will also remind them of the intentionality of model design. I do not plan to spend much time reviewing the immune system, as we will have covered this in depth, so I do not plan on asking my students to complete any of question 2. I will also remove part of question 3 and all of question 4. For time's sake, I do not intend to ask students the questions that pertain to Part II, but will use it as an introduction to the next section. The reason I am particularly excited about the remainder of this activity is because it requires students to use their science skills to understand immunological advantages that some individuals have against HIV. It uses actual data from research studies and has students interpret the methodologies, make predictions, and interpret results. All of these methods build science skills while also preparing students to interpret more in-depth scientific papers that they may encounter later in life. Students should complete this activity with a thorough understanding of the structure of HIV and impact that it has on the human immune system. They should be able to use both of these concepts to explain why some individuals have observed immunity or stronger defenses against HIV infection and, thus, AIDS contraction.

While the case study will provide students with a detailed understanding of genetic mutations that provide advantages to certain individuals, I want to make sure that my students are also able to discuss the various aspects of HIV that make it so evasive to scientists who are trying to create vaccines for the general public. The students will participate in a jigsaw reading activity with their lab groups. This will also require students to dive into a vocabulary heavy research study and identify main ideas of certain sections. Different groups will receive a section from "Implications of Recombination on HIV diversity" by Ramirez et al. Each group will be assigned one of the following sections to read and interpret: Introduction (Section 1), Recombination in HIV: requirements and mechanistic outputs (Section 2), HIV Classification and Figure 2 Interpretation (Section 3.1), Recombinant forms in the epidemics & Limits to recombination (Sections 3.2 & 3.3), and Recombination, the host, and antiviral treatments (Introduction to Section 5). The level of reading in this article will be extremely challenging for students. They will be asked to work in groups to grasp the main idea without worrying about the specific details. Once all groups have shared the main idea of their reading with the entire class, I will ask

the class to answer the following questions:

- "What factors allow HIV to evade the immune system?"
- "How do these attributes make it difficult to create a vaccine?"
- "How do the mechanisms described relate to evolution as a driving force?"
- What implication might the geographic distribution of HIV genetic forms have on vaccine development?

This cycle should take approximately 5 days to complete but will thoroughly prepare students to discuss why it has been so difficult for scientists to create a vaccine to prevent the spread of HIV. They should be able to create a model of an HIV vaccine and its infection of human immune cells, articulate all of the ways that HIV is able to evade the immune system, and describe the ways in which some people have increased defense or even immunity against HIV.

Activity Five: Culminating Socratic Seminar

The culminating activity of this unit will be a Socratic seminar in which students will revisit all essential questions and will formulate all concepts learned throughout the unit to draw some relevant conclusions about HIV and vaccines. Before students participate in the seminar, they will be given one of two readings. The readings include an NBC News article written by Dr. Anthony Fauci entitled "Fauci: Why there is no AIDS vaccine" and a reading from the resource library of the Understanding Evolution website created by the University of California's Museum of Paleontology entitled "A chink in HIV's evolutionary armor." Both of these articles have different approaches to the progress made and challenges faced by scientists trying to develop an HIV vaccine. Students will be required to write a brief summary of the article in preparation for the discussion and will need to write out talking points for each of the essential questions of the unit.

In the true sense of a Socratic seminar, it will be the responsibility of students to lead the discussion, incorporate the readings, and refer to concepts that were learned. My goal is to encourage them to use all of the resources they accessed to learn the concepts in their discussions about background and next steps. To stimulate the conversation, I will also ask extension questions or provide prompted reminders to students at advantageous times. For example, I will remind them about the reference in *A Planet of Viruses* to the Merck vaccine that was developed and abandoned. If students do not remember this, they will have access to the text to look it up. I will also ask them if, based on what they learned about more virulent diseases like Ebola hemorrhagic fever, whether it would be ethically acceptable to genetically modify HIV so that it would become more virulent? A prompt like this will require students to activate their understanding of the concepts that apply and make connections between multiple activities. It is likely that a Seminar such as this one will not find resolution. However, before the class ends, I will present them with the news article from Huffington Post released in September, 2013 entitled "HIV Vaccine: Western University Researchers Report Success in Trials." If time remains in class, students will have a chance to reflect on the article. Otherwise, I will encourage students to react to the article on our class webpage. My hope is that by ending the unit in this manner, students will have an opportunity to demonstrate their full understanding of the content learned but will also become more active citizens by engaging in discussions around a very real, and relevant, concern in the scientific community.

Notes

1. "The Future is Here: GWCP Brochure."

2. "Illinois State Report Card: Westinghouse High School."

3. Danilova, "Evolution of Immune Mechanisms," 513

4. Mader and Windelspecht, *Biology*, 631

5. Ibid., 630-632

6. Ibid., 633-639

7. "Immunology Module: Humoral Immunity."

8. Mader and Windelspecht, *Biology*, 633-639

9. Fauci, "Fauci: Why there is no AIDS vaccine"

10. Riedel, "Edward Jenner", 21

11. Ibid.

12. Ibid.

13. Ibid., 23

14. Ibid., 24-25

15. Zimmer, *Planet of Viruses*, 5

16. Ibid.

17. Ibid., 45

18. Mader and Windelspecht, *Biology*, 365-366

19. Zimmer, *Planet of Viruses*, 5

20. Ibid., 90

21. Blerkom, "Role of Viruses," 18

22. Mader and Windelspecht, *Biology*, 365-368

23. Zimmer, *Planet of Viruses*, 5

24. Ibid., 52

25. Sanjuan, et al., 9738

26. Ibid., 9733-9737

27. Blerkom, "Role of Viruses," 22

28. Ibid., 28

29. Ibid., 22

30. Mansky, "Retrovirus mutation rates," 1340

31. Blerkom, "Role of Viruses," 22-23

32. Ibid., 15

33. Ibid., 32

34. Ibid., 15

35. Zimmer, *Planet of Viruses*, 52

36. "CDC HIV/AIDS: Basic Statistics."

37. Ibid.

38. Chicago Department of Public Health, "HIV/STI Surveillance," 5

39. Ramirez et al., "Implications of recombination", 64

40. Ibid., 65

41. Zimmer, *Planet of Viruses*, 58

42. Ibid., 59-60

43. Ramirez, et al., "Implications of recombination," 66

44. Ibid., 66-67

45. Zimmer, *Planet of Viruses*, 61

46. Ibid.

47. "CDC HIV/AIDS: HIV Among Youth."

48. Fauci, "Fauci: Why there is no AIDS vaccine"

49. Zimmer, *Planet of Viruses*, 61

50. Fauci, "Fauci: Why there is no AIDS vaccine"

51. Ibid.

52. Mansky, "The mutation rate of Human Immunodeficiency Virus Type 1," 391

53. Lanciault and Champoux, "Pausing during Reverse Transcription," 2483

54. Song et al., "Impact of immune escape," 2-3

55. Ibid., 7

56. "Understanding Evolution: A chink in HIV's evolutionary armor"

57. Fauci, "*Fauci: Why there is no AIDS vaccine*"

58. Ibid.

59. Ibid.

60. Hütter et al., "Long-Term Control of HIV by CCR5", 692-698

61. Fauci, "*Fauci: Why there is no AIDS vaccine*"

Bibliography

1. "B Cell Activation." Wikimedia Commons. http://commons.wikimedia.org/wiki/File:B_cell_activation.png (accessed August 12, 2014).

2. Blerkom, Linda M. Van. "Role of viruses in human evolution." *American Journal of Physical Anthropology* 122, no. S37 (2003): 14-46.

3. Centers for Disease Control and Prevention. "Basic Statistics." Centers for Disease Control and Prevention. http://www.cdc.gov/hiv/basics/statistics.html (accessed July 13, 2014).

4. Centers for Disease Control and Prevention. "HIV Among Youth." Centers for Disease Control and Prevention. http://www.cdc.gov/hiv/risk/age/youth/index.html?s_cid=tw_drmermin-00186 (accessed July 15, 2014).

5. Chicago Department of Public Health. "HIV/STI Surveillance Report, Chicago." City of Chicago. http://www.cityofchicago.org/content/dam/city/depts/cdph/infectious_disease/STI_HIV_AIDS/HIV_STISurveillanceReport2013.pdf (accessed July 15, 2014).

6. Danilova, Nadia. "The evolution of immune mechanisms." *Journal of Experimental Zoology Part B: Molecular and Developmental Evolution* 306B, no. 6 (2006): 496-520.

7. Fauci, Anthony. "Fauci: Why there is no AIDS vaccine." NBC News. http://www.nbcnews.com/id/29898087/ns/health-aids/t/fauci-why-there-no-aids-vaccine/ (accessed July 15, 2014).

8. Fisher, Patrick. "Immunology Module." Prologue home.

http://missinglink.ucsf.edu/lm/immunology_module/prologue/prologuehome.html (accessed July 15, 2014).

9. "HIV Vaccine: Western University Researchers Report Success In Trials." The Huffington Post. http://www.huffingtonpost.ca/2013/09/04/aids-hiv-vaccine-western-university_n_3865059.html (accessed July 15, 2014).

10. Hutter, Gero, Daniel Nowak, Igor W. Blau, Wolf K. Hofmann, Eckhard Thiel, Maximilian Mossner, Susanne Ganepola, Arne MuBig, Kristina Allers, Thomas Schneider, Jorg Hofmann, Claudia Kucherer, and Olga Blau. "Long Term Control of HIV by CCR5 Delta32/Delta32 Stem-Cell Transplantation." *The New England Journal of Medicine* 360 (2009): 692-698.

11. Illinois State Board of Education. "Report Card: George Westinghouse College Prep." Illinois State Report Card. http://www.illinoisreportcard.com/School.aspx?source=Profile&Schoolid=150162990250857 (accessed July 15, 2014).

12. Lanciault, Christian, and James J. Champoux. "Pausing during Reverse Transcription Increases the Rate of Retroviral Recombination." *Journal of Virology* 80, no. 5 (2006): 2483-2494.

13. Mader, Sylvia S., and Michael Windelspecht. *Biology*. 11th ed. New York: McGraw-Hill, 2013.

14. Mansky, Louis M.. "The Mutation Rate of Human Immunodeficiency Virus Type 1 Is Influenced by the vpr Gene." *Virology* 222, no. 2 (1996): 391-400.

15. Mansky, Louis M.. "Retrovirus mutation rates and their role in genetic variation." *Journal of General Virology* 79 (1998): 1337-1345.

16. National Institute of Allergy and Infectious Diseases. "HIV/AIDS." More on How HIV Causes AIDS, NIAID, NIH. http://www.niaid.nih.gov/topics/hivaids/understanding/howhivcausesaids/pages/howhiv.aspx (accessed July 15, 2014

17. Ramirez, Bertha Cecilia, Etienne Simon-Loriere, Roman Galetto, and Matteo Negroni. "Implications of recombination for HIV diversity." *Virus Research* 134, no. 1-2 (2008): 64-73.

18. Riedel, Stefan. "Edward Jenner and the history of smallpox and vaccination." *Baylor University Medical Center Proceedings*, January 1, 2005.

19. Sanjuan, Rafael, Miguel R. Nebot, Nicola Chirico, Louis M. Mansky, and Robert Belshaw. "Viral Mutation Rates." *Journal of Virology* 84.19 (2010): 9733-9748.

20. Song, Hongshuo, Josh Eudailey, Mark S Drinker, Bhavna Hora, Anna Berg, Jeffrey W Pavlicek, Fangping Cai, Tanmoy Bhattacharya, Hui Li, Shilpa S Iyer, Katharine J Bar, Julie M Decker, Joy Pickeral, Nilu Goonetilleke, Michael Kp Liu, Feng Gao, M Moody, Guido Ferrari, Andrew Mcmichael, Alan S Perelson, George M Shaw, Beatrice H Hahn, and Barton F Haynes. "Impact of immune escape mutations on HIV-1 fitness in the context of the cognate transmitted/founder genome." *Retrovirology* 9, no. 1 (2012): 89.

21. "T Cell Activation." Wikimedia Commons. http://commons.wikimedia.org/wiki/File:T_cell_activation.png (accessed August 12, 2014).

22. "The Future is Here: GWCP Brochure." Westinghouse College Prep. http://newwestinghouse.org/apps/pages/index.jsp?uREC_ID=56511&type=d&termREC_ID=&pREC_ID=396923&hideMenu=1 (accessed July 15, 2014).

23. University of California Museum of Paleontology. "A chink in HIV's evolutionary armor." Understanding Evolution.

http://evolution.berkeley.edu/evolibrary/news/070301_hiv (accessed July 15, 2014).

24. Zimmer, Carl. *A planet of viruses*. Chicago: University of Chicago Press, 2011.

Resources for Teachers

Wordle

The wordle that I already created for this unit can be found at:

http://www.wordle.net/show/wrdl/7994486/AP_Biology_Viruses

You can create your own wordle at:

http://www.wordle.net

Immunology Module

The following includes an interactive module that introduces the immune system. The module was designed by Patrick Fisher, a previous student of the UCSF School of Medicine, and was last updated in 2008.

http://missinglink.ucsf.edu/lm/immunology_module/prologue/prologuehome.html

Todays Meet:

https://todaysmeet.com/

"Resistance is Futile—Or is it?: The Immunity System and HIV Infection" Case Study

The referenced case study along with teacher resources can be found at:

http://sciencecases.lib.buffalo.edu/cs/collection/detail.asp?case_id=393&id=393

It is also available in a clicker version. Additional case studies can be found at the National Center for Case Study Teaching in Science can be found at their home page:

http://sciencecases.lib.buffalo.edu/cs/

Appendix: Implementing District Standards

The following is not an exhaustive list of standards and objectives addressed in the unit. It does include standard alignment for the AP Biology framework, Common Core State Standards, and College Readiness Standards.

AP Biology Standards (from the AP Biology Framework created by College Board)

Standards have been condensed for the purpose of space. An expanded version of these skills can be found in the AP Biology Curriculum Framework.

Big Idea 1: Enduring Understanding 1.A.

Essential knowledge 1.A.4.b.3

Big Idea 2: Enduring Understanding 2.D

Essential knowledge 2.D.4.a; 2.D.4.b.1-6

Big Idea 3: Enduring understanding 3.A

Essential knowledge 3.A.1.a.5; 3.C.3.a.1-6; 3.C.3.b.1-2;

Learning Objectives: 3.29-30

Common Core State Standards

CCSS.ELA.RST.11-12: 1, 2, 4, 7, 9, 10

College Readiness Standards (Developed by ACT)

SIN24-27.2 Understand a complex experimental design

SIN24-27.3 Predict the results of an additional trial or measurement in an experiment

EMI24-27.6 Select a data presentation or a model that supports or contradicts a hypothesis, prediction, or conclusion

EMI28-32.1 Select a complex hypothesis, prediction, or conclusion that is supported by a data presentation or model.

EMI 28-32.2 Use new information to make a prediction based on a model.

The AP Biology standards focus on the content that is taught through the unit. The Common Core State Standards and College Readiness Skills are literacy and scientific thinking skills whose development is supported through the instructional strategies presented.
