

# Retro Goes Modern: The Evolution and Evasive Maneuvers of HIV

by

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## Introduction

As nonliving entities, viruses face specific challenges when replicating in a host. Avoiding the host immune system is something that every virus must face in order to successfully reproduce itself and infect another host. Human immunodeficiency virus (HIV) is unique in many ways, making it especially interesting to study the concepts of immune evasion. As a member of the Retroviridae, HIV is a single-stranded RNA virus that is capable of reverse transcribing itself into DNA to insert itself into the host genome, thus stretching our concept of biology's central dogma. Additionally, HIV infects cells of the host immune system and has many genes that are responsible for immune evasion strategies. Finally, HIV's incredible mutation rate causes the immune system to constantly change its tactics in fighting off the infection.

For the next two class periods, we will investigate this topic. In order to prepare for class, we have provided a set of short articles and some questions to start you thinking about how HIV evolved, how it infects humans, and the challenges behind current treatments and future cures. The main article that we will read is a short communication that details the recent spread of a new strain of HIV from gorillas to a woman in Cameroon, Africa. Along with the original article, you will also read a few popular press releases about the research. As you read, pay attention to the accuracy of the popular press articles compared to the original paper. Are depictions accurate? Is anything misleading? Do the popular press articles emphasize the same points or do they differ? Keep this in mind as you work through the content questions and scenarios over the next two days.

## Homework for Day 1

Based on the knowledge you have gained in class, answer the following questions to prepare yourself for the first day of the HIV case study:

1. How does HIV replicate?
2. What is the typical immune response to a viral infection?
3. How does SIV differ from HIV?

Also in preparation, please read the following very short articles about a new strain of HIV that was recently discovered:

1. "Researchers identify new strain of HIV derived from gorillas" by Arthur Brice (*CNN*).
2. "New HIV strain originated in gorillas" by Lynne Peeples (*Scientific American Blog*).
3. Plantier J-C et al. 2009. A new human immunodeficiency virus derived from gorillas. *Nature Medicine* 15(8): 871–872.

*Day 1: Part 1*

For homework you read two popular press articles and one scientific article about the emergence of a new strain of HIV from gorillas. Based on your in-class knowledge, the content of the articles, and any other sources that you can utilize, answer the following questions:

1. How does the genomic structure of SIV compare with HIV?
2. How many different strains of HIV exist? Where do they come from?
3. What is the evidence that this is a totally new strain of HIV?
4. How is HIV transmitted? How is it thought that this new strain was transmitted from gorillas to humans?
5. Many viruses pass freely between different host species, including influenza, rabies, and cowpox. Based on your knowledge of SIV and HIV structure, is there strong evidence for the directionality of spread of HIV to humans from non-human primates infected with SIV? Why or why not? Could humans spread HIV to primates?
6. Do you think that there is sufficient evidence to believe that this new strain is a minor variant with low overall impact on the human population? Why or why not?
7. Do the popular press articles faithfully describe the content of the primary research article? Why or why not?

*Day 1: Part 2*

1. How does HIV infect its host?
2. How does mode of transmission impact the infectivity of the virus? What immune cells would be impacted with each transmission mode?
3. Looking at the structure of HIV, what do you predict would be its immunodominant antigens?
4. What is the rate of mutation of HIV, and how does this impact viral infectivity and the host immune response?
5. How does the new strain of HIV from gorillas (“P” variant) replicate compared to other strains? What would this mean for how the virus acts within the host?
6. Your friend has a genetic mutation that he says ensures he will never catch HIV. A mutation in CCR5 is carried in the descendants of Northern Europeans. Why is this mutation prevalent and how does it cause resistance? Is your friend correct that he doesn’t have to worry about being exposed to HIV?

*Homework for Day 2*

Please answer the following questions in preparation for Day 2 of our case study on HIV.

1. What immune evasion genes does HIV have?
2. What determines the onset of AIDS?
3. Does HIV itself kill patients?

Also, please read the following short articles to prepare for our discussion:

1. “Gorillas have been found, for the first time, to be a source of HIV” (BBC News 2009)
2. “Gorilla-derived HIV: A warning to public health practitioners” (Health and Human Rights Blog, 2009)
3. HIV Drug Resistance Fact Sheet (World Health Organization, April 2011)

*Day 2: Part 1*

1. Consider the popular press articles that you read for homework the past two nights. How do the stances of the articles from the Day 2 readings differ from the articles you read for Day 1?
2. Does this new information change your opinion on the impact of P variant HIV strains that you formulated on Day 1? Why or why not?
3. Often people must wait at least six weeks after suspected exposure before getting an HIV test. Why is this waiting period necessary?
4. What types of testing are available for HIV? Are these tests able to detect all HIV strains? Why or why not?
5. What drugs are available to treat people with HIV infections? How do these drugs act to reduce viral load? Would these drugs work on all variants of HIV?
6. Last time you learned about the mutation rate of HIV. What effect might the mutation rate have on the development of HIV drug resistance? Is there evidence for this occurring?
7. An HIV patient develops multidrug resistance while taking a cocktail of anti-retroviral chemotherapeutics. His doctor decides to remove him from the drugs because they are expensive and are not working. What do you predict might happen to the virus upon removal of the drugs? If the patient were to receive another round of drugs at a later date, would they be effective? Why or why not?

*Day 2: Part 2*

1. How is HIV able to circumvent the immune response?
2. In someone with full-blown AIDS, what immune system components are still intact? What does this do to their susceptibility to infection?
3. What antigen(s) would you utilize to create an HIV vaccine? Why did you choose these candidates?
4. An HIV vaccine trial in 2008 abruptly ended due to the observation that participants who received the vaccine contracted HIV at a higher rate than those receiving placebo. Explain why this could happen.



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