Lesson 2

HIV Structure/Life Cycle and Implications for Vaccine Development

OVERVIEW

Purpose

Prior to beginning content, the students will be introduced to their final assessment projects, including the vaccine trial proposal and reflection paper. This lesson will review with students the general structure and life cycle of the HIV virus. It will introduce them to the idea of identifying places within the life cycle to be interrupted by a vaccine.

Essential Understandings

Mutations in viruses force the immune system to adapt and respond; vaccines must also stimulate an immune response. Since there is no history of a human being naturally clearing an HIV infection, a vaccine must produce an immune response which is better than that currently produced by the body.

Learning Objectives:

- Students will gain a greater understanding about the structure and life cycle of HIV
- Students will apply their understanding about the life cycle of HIV to identify targets of interruption
- Students will be able to explain how mutations occur and why they can create challenges to developing effective vaccines

Key Concepts

HIV Structure and Life Cycle

Prior Knowledge Needed

Basic HIV/AIDS background information

Immune system and how vaccines work in the immune system

Materials

Overhead projector or LCD Projector (optional)

Computer Lab for students

Paper and pencils

Copies of Student Worksheets

Prep Time

Teacher may want or need to do some background reading so they are comfortable with the content area of HIV structure and life cycle.

Prepare copies and overhead transparencies if necessary

Class Time

1-2 days depending on the depth and level of discussion

Timeline:

- 1 week before activity:
  - Reserve computer lab
  - Make copies of student handouts

Extensions

- Investigate naturally occurring mutations that make people resistant to HIV infection
- Explore possible links between resistance to HIV and survival of historical diseases such as Black Plague
- Have students write and create a children's story book with diagrams to teach and illustrate the HIV virus life cycle and how it has been able to evade researchers in developing a vaccine.

Adaptations

- Make a Power Point presentation to explain HIV life cycle and relate it to the viruses ability to evade researchers attempts to engineer an effective vaccine.
- See Day One for ELL and IEP adaptations

Assessment Suggestions

- Review WebQuest answers
- Monitor students responses during debrief and discussion
- Analyze responses given in reflective paragraphs

Common Misconceptions

- HIV+ people are all infected with the same virus
- A vaccine has not been developed because of government conspiracy
- The only reason a vaccine has not been developed is because not enough funding is available

ADDITIONAL RESOURCES

- See Appendix for
  - Review of HIV – Background
  - HIV Life Cycle Review Materials
- See Appendix for Selected Possible Interventions of HIV Life Cycle (within HIV Sample Lesson)
- HIV Life cycle – Additional Animation
  - **http://www.learner.org/channel/courses/biology/units/hiv/index.html**
    This very helpful website has animations detailing the immune system, HIV infection, HIV receptors, and the HIV DNA vaccine. It also has a number of still images, expert interviews and an online textbook.
  - **www.roche-hiv.com/Newsandfeatures/animations/animations_multimedia.cfm**
    Short animations including HIV lifecycle, fusion and cell entry, attachment inhibition, co-receptor inhibition, and fusion inhibition
  - **www.roche-hiv.com/Newsandfeatures/animations/lifecycle/lifecycle_animation.cfm?link=HIVTreatment**
    No discussion of mutations but good information and good step-by-step animations
  - **www.cellsalive.com/hiv2.htm**
    This contains some good information but is somewhat dated and has information that is still being debated

Lesson 2 Activities

SUMMARY

2.1. Explanation of Final Assessment Projects

Option A –Individual Essay

Each student will be expected to write a paper explaining the basics of HIV vaccine development. They will be writing paragraphs of this paper following each lesson and then compiling them into a final product.

Option B – Group Research Proposal Presentation

As a group, students will assume the role of scientists and design a vaccine strategy for a Phase I trial. They will need to identify the HIV life cycle target and recommend a population for testing. Be sure students understand more information will follow.

Option C – Research Proposal Review as a member of an Institutional Review Board

Working either individually or as a group, students review a mock research proposal seeking to gain IRB approval. The IRB evaluates whether or not the research proposed should proceed.

2.2 Invitation to Learn

1. Play Roche animations for the class
   - **www.roche-hiv.com//Newsandfeatures/animations/animitions_multimedia.cfm**
   - **www.roche-hiv.com/Newsandfeatures/animations/lifecycle/lifecycle_animation.cfm?link=HIVTreatment**
2. How would a vaccine or treatment interrupt the life cycle of HIV?

2.3 HIV Life Cycle WebQuest

1. Choose one of the following websites and have students complete companion worksheet in pairs. *Note: Can show NOVA animation to the class and then have students complete worksheet for second animation in pairs.*
   - **www.pbs.org/wgbh/nova/aids/action.html**
     - Good animation about life cycle but does not discuss mutations
     - Be sure to stress mutations during debrief discussion
   - **www.sumanasinc.com/webcontent/anisamples/majorsbiology/lifecyclehiv.html**
     - contains information specific to mutation of HIV on slide 4

Symbols

— video
— discussion
— hands-on
— on-line or web based
— homework

2. For teachers without access to computer labs or LCD Projectors:

- Give students worksheet to complete as teacher shows the animations to the class
- Print copies of the animation slides and use as transparencies; walk through and aid students in completing the worksheet

2.4 Debrief and Discussion

1. Teacher should facilitate debrief of worksheets with the students. Be sure to reference final assessment projects. Encourage discussion of the following:

- Mutations of HIV and implications for vaccine development
- Cells targeted by HIV and implications for body response
- Possible places of interruption of life cycle for treatments or vaccines

2.5 HIV Vaccine Expository Paragraphs

1. Ask students to write 1 paragraph about each of the following for homework:
    - Describe the structure and life cycle of HIV
    - What are possible targets for interrupting the HIV life cycle?

2.6 Homework Reading Assignment

- Have students read "HIV Vaccines Explained" by the US Department of Health and Human Services Feb. 2004. This provides background information to set the stage for Day Three.
    - See the end of Lesson 3 for the hardcopy
    - www2.niaid.nih.gov/Newsroom/mayday/pdf/HVAD2005_HIVvaccinebrochure.pdf

Teacher Information

HIV Life Cycle WebQuest

In order to give students a greater understanding of the life cycle of HIV, animations or diagrams are suggested. There are two websites below with suggestions (and student worksheets) to be used with each.

www.pbs.org/wgbh/nova/aids/action.html

- Give students worksheet and allow them to use computers to complete; discuss as a class when finished
- Give students worksheet and use LCD projector or other method to show students the website from one class computer; discuss and complete worksheet together

www.sumanasinc.com/webcontent/anisamples/majorsbiology.lifecyclehiv.html

- Give students worksheet and allow them to use computers to complete; discuss as a class when finished
- Give students worksheet and use LCD projector or other method to show students the website from one class computer; discuss and complete worksheet together
- Print out slides and convert to Transparencies and walk through as students complete worksheet

NAME_____ Date_____ Period_____

The HIV Life Cycle WebQuest

Use the website **http://www.pbs.org/wgbh/nova/aids/action.html** to answer the following questions about the HIV virus.

Click on Viral Entry

1. To what cell type does the HIV virus attach itself?

2. Explain how HIV is able to enter these cells.

3. How important are the receptors on the cell membrane to HIV entry? Why?

4. Why do some HIV+ individuals show no sign of the disease?

Click on Viral Gene Transfer

5. What must RNA do before it can become incorporated into the host cell's DNA?

6. How are new viral proteins built using the host cell's machinery?

Click on Viral Exit

7. How is HIV spread inside the body?

8. Why are HIV patients susceptible to other infectious agents?

Wrap-up Question

9. Based on what you have learned, hypothesize why it is so difficult for the human body to fight HIV like it does other viruses.

The HIV Life Cycle WebQuest

Use the website **http://www.pbs.org/wgbh/nova/aids/action.html** to answer the following questions about the HIV virus.

Viral Entry

1. To what cell type does the HIV virus attach itself?

   The animation shows an HIV particle attaching itself to a lymphocyte. Lymphocytes, which include helper T cells and killer T cells, are small white blood cells that are critical in immune defense and are HIV's principal target. (HIV can also attach itself to macrophages, which also have CD4 receptors on the surface. Macrophages are large white cells whose job it is to "clean up" foreign material by engulfing it.)

2. Explain how HIV is able to enter these cells.

   The binding process is facilitated by a molecule on the surface of the HIV particle called gp120. Gp 120 binds to two chief receptors (CD4 and CCR5) on the outside of the host cell, much like a key fitting into a lock. Once the viral particle has successfully binded to the host cell, its core can pass through the cell wall into the cell's cytoplasm.

3. How important are the receptors on the cell membrane to HIV entry? Why?

   Very important. If the HIV particle can't bind with the host cell, it can't enter the cell and insert its RNA inside the host cell. (It is not mentioned in the animation, but some HIV has adapted to use a different co-receptor, CXCR4)

4. Why do some HIV+ individuals show no sign of the disease?

   They may be missing the gene (or have mutations in the gene) that makes the CCR5 receptor, so that a defective protein or no protein is made. Without this receptor, the HIV particle does not fully bind and cannot easily enter the host cell.

Viral Gene Transfer

5. What must RNA do before it can become incorporated into the host cell's DNA?

   It must form a double-stranded viral DNA using the single-stranded viral RNA as a template. It uses an enzyme known as reverse transcriptase to help do this.

6. How are new viral proteins built using the host cell's machinery?

   The viral DNA integrates itself into the host's DNA. The DNA is then transcribed into RNA, which migrates out of the nucleus (which houses the host's DNA) into the cytoplasm. There, new viral proteins are built using the viral RNA as a blueprint. More specifically (and not mentioned in the animation), the RNA is translated into viral proteins using the host's ribosomes, amino acids, and cellular machinery to make these building blocks that can then self assemble into new virus particles.

Viral Exit

7. How is HIV spread inside the body?

   The new HIV particles move out of the cell, where they head off to infect other cells and perpetuate the life cycle. This process repeats itself continuously, with many thousands of HIV particles produced simultaneously in the body.

8. Why are HIV patients susceptible to other infectious agents?

   After repeated assaults by viral particles, very key host cells (CD4 T helper cells) die, having exhausted their energy and molecular building supplies while generating HIV viruses. This suppresses a patient's immune system and leaves him or her open to infection by other infectious agents, including bacteria, fungi, and other viruses.

Wrap-up Question

9. Based on what you have learned, hypothesize why it is so difficult for the human body to fight HIV like it does other viruses.

   HIV attacks the very system (the immune system) that protects the body from foreign invaders.

NAME_____ Date_____ Period_____

The HIV Life Cycle

Use the following website to answer the following questions about the HIV virus.

http://www.sumanasinc.com/webcontent/anisamples/lifecyclehiv.html

You may use step-through or narrated to complete this worksheet. You may find that using the narrated first, and then following with the step-through will be the best way to get the most information.

1. Explain, in as much detail as possible, how the HIV virus enters a cell.

2. Name the part of HIV that interacts with the receptor on the host cell. What is the name of the host cell receptor?

3. What happens to the lipid membrane of the virus?

4. Which parts of HIV enters the cell? Which parts remain outside the cell?

5. List the organelles the animation shows inside the host cell.

6. What converts the viral RNA into DNA?

7. Why is there a high mutation rate in HIV?

8. Describe the role of integrase. Why is it so important for HIV?

9. Based on what you already know about genetics, what does it mean for the host cell, now that the viral DNA has become a part of the Host Cell Genome?

10. Summarize the steps between integration of the viral DNA into the host DNA and assembly of new viral particles.

11. What is unique about how HIV viral particles exit the host cell? (Hint: What do they take with them???)

12. Based on what you have learned, hypothesize why it is so difficult for the human body to fight HIV like it does other viruses.

The HIV Life Cycle

Use the following website to answer the following questions about the HIV virus.

http://www.sumanasinc.com/webcontent/anisamples/lifecyclehiv.html

1. Explain, in as much detail as possible, how the HIV virus enters a cell.

   HIV has surface proteins called gp120 that attach to cells that have CD4 receptors on their surfaces. CD4 is found on the immune system's helper T (T_H) lymphocytes and on scavenger cells called macrophages. The binding to CD4 proteins and other cell-surface proteins, called co-receptors (not shown in the animation) allows the virus to fuse with the cell. The lipid membrane of the virus incorporates into the cell's membrane, while the viral core enters the host cell.

2. Name the part of the HIV virus that interacts with the receptor on the host cell. What is the name of the host cell receptor?

   The gp120 is the part of HIV that interacts with the CD4 receptors (and co-receptors not shown on the animation) on the host cell.

3. What happens to the lipid membrane of the virus?

   It gets incorporated into the membrane of the host (helper T or macrophage) cell.

4. Which parts of HIV enters the cell? Which parts remain outside the cell?

   The viral core, which has the RNA and some copies of reverse transcriptase inside it, enters the host cell. The lipid membrane becomes incorporated into the host's membrane.

5. List the organelles the animation shows inside the host cell.

   The animation shows the nucleus, rough endoplasmic reticulum (ER), and Golgi apparatus. The cell membrane and cytoplasm are sometimes considered organelles.

6. What converts the viral RNA into DNA?

   The enzyme reverse transcriptase copies the RNA into complementary DNA, then the enzyme ribonuclease H destroys the original RNA strand. Reverse transcriptase then synthesizes a second DNA strand using the first strand as a template.

7. Why is there a high mutation rate in HIV?

Reverse transcriptase has a high error rate and frequently leaves mutations in the copied DNA. The mutations result in variant forms of HIV which a) allow HIV to evolve quickly (as shown in the animation), or b) cause the virus to be inactive (not shown in the animation).

8. Describe the role of integrase. Why is it so important for the HIV virus?

Integrase enzymes splice the viral DNA into the host cell's chromosomal DNA. The viral DNA must be spliced into the host DNA so that the host cell can be commandeered to make HIV components for new viral assembly.

9. Based on what you already know about genetics, what does it mean for the host cell, now that the viral DNA has become a part of the Host Cell Genome?

Once the viral DNA is integrated into the host cell DNA, it becomes part of that cell's own genome. It is no longer "foreign" and cannot be distinguished from the cell's original DNA.

10. Summarize the steps between integration of the viral DNA into the host DNA and assembly of new viral particles.

The viral DNA that has been incorporated into the host DNA instructs the cell to make viral RNA strands. These RNA strands contain the information to produce full-length viral RNA molecules, capsid proteins, envelope proteins other proteins needed for viral assembly. All of the components gather at the membrane and assemble to become complete viruses. They then bud off from the host cell.

11. What is unique about how HIV viral particles exit the host cell? (Hint: What do they take with them???)

They coat themselves with pieces of the cell's own membrane.

12. Based on what you have learned, hypothesize why it is so difficult for the human body to fight HIV like it does other viruses.

HIV infects the very cells in the immune system which are programmed to fight off foreign invaders. With a destroyed immune system, the body is vulnerable to a host of diseases.

Although HIV does have some components of the host cell, it is recognized as foreign, and the immune system makes a strong immune response to it. The reason that it cannot be easily eliminated is for two major reasons: (1) the viral proteins are constantly changing and "escaping" the immune response; and (2) because the virus is integrated into the host's DNA, viruses are produced continuously through the life of the infected patient.