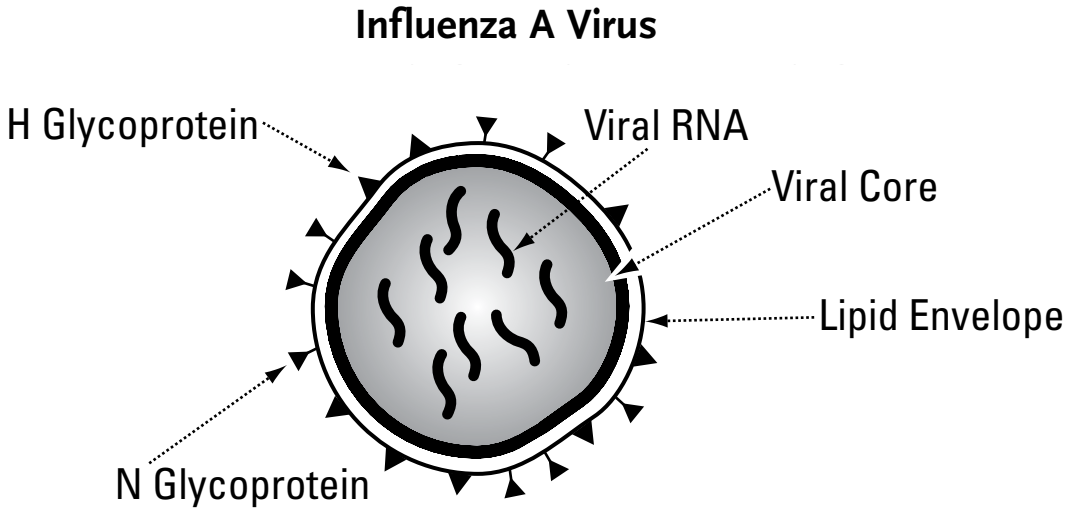
Modeling an Avian-Human Hybrid Flu Virus

Students learn about the structure of influenza A viruses, how they replicate in a cell, and how their RNA can reassort when a person is infected simultaneously with an avian and a human virus. Using the student sheet, students make avian and human influenza A virus models, infect a model lung cell, and make a hybrid virus that has some avian and some human RNA segments. They see that some hybrids have surface proteins from both the avian and human influenza A viruses. Unfortunately, the human immune system does not quickly recognize and respond to this combination of surface proteins, making it particularly dangerous.

Background Information

While there are three main types of influenza viruses (Types A, B, and C), this activity focuses on influenza A and its strains. Influenza A in humans is mainly a respiratory virus that typically infects cells of the nose and throat, but it can infect lung cells. It spreads when an uninfected person touches contaminated surfaces or inhales viruses coughed or sneezed out by an infected person.



Viruses have a simple composition. They are made of DNA or RNA; they have no metabolism or organelles; and they use the host cell (the cell they infect) to multiply. The human Influenza A and B viruses have eight single-stranded RNA segments in a protein shell. The RNA and its surrounding protein is called the viral core. The core is surrounded by a lipid covering that has surface glycoprotein spikes called H (hemagglutinin) and N (neuraminidase).

Influenza A infects humans and animals such as birds, pigs, horses, and seals. When it infects birds, it is called avian influenza; when it infects pigs, it is called swine influenza, and so on. Typically, avian influenzas infect birds. But occasionally, avian influenza infects humans who have been in close contact with birds.

The recent avian strain that has been infecting humans is called H5N1 (named for its surface glycoproteins). H5N1 kills a high percentage of people who become infected, but thus far, the virus does not seem to spread well from person to person. Scientists fear that a person already infected with a human influenza A virus may become infected with the avian influenza A. If infected with both viruses, a hybrid avian-human influenza A virus may be generated that has two features making it particularly dangerous for humans: avian H and N glycoproteins, to which humans have never been exposed (thus the immune system cannot quickly recognize and control the virus), and RNA from the human virus (enabling the hybrid to spread easily from person to person).

For a global outbreak of influenza to occur, three conditions must be met: a new virus subtype must arise; this subtype must be able to cause serious illness in humans; and it must spread easily from person to person—and continue to do so. The first two conditions have been met with H5N1 human infections. Scientists are working to better understand different influenza A strains in hopes of preventing the spread of this virus.

One way virologists identify influenza A strains that could potentially cause a pandemic is by infecting cells simultaneously with different influenza strains and analyzing the hybrid viruses produced. Once strains are identified, the researchers can work on developing vaccines for them.

Materials (for each team)

- Student activity sheet: *Modeling an Avian-Human Hybrid Flu Virus*
- quart-size plastic bag
- pint-size plastic bag
- 2 plastic novelty eggs shells that come apart
- 8 paper clips and 2 small rubber bands, all of one color
- 8 paper clips and 2 small rubber bands, all of one color but a different color than the first set
- tape or small labels
- 2 film containers

Standards Connection

Science Standard C: Life Science

- Grades 5–8. Structure and Function in Living Systems
- Grades 9–12: The Cell

Science Standard F: Science in Personal Perspectives

- Grades 5–8. Risks and Benefits
- Grades 9–12: Personal and Community Health

Video is not required for this activity.

Procedure

1. Tell students that viruses cause colds, polio, flu, AIDS, hepatitis, measles, chicken pox, and cold sores. Explain that there are many different groups of viruses, but they all share similar characteristics. Have student pairs write their best definition of a virus. As the class shares its definitions, create an accurate virus definition by writing on the board the parts that are true. Discuss the differences between viruses, bacteria, and eukaryotic cells. *(Viruses depend on the host cell to replicate; bacteria are generally single-celled organisms that do not rely on a host cell to reproduce; and most eukaryotic cells have a nucleus that contains the genetic material.)*
2. Ask students to share what they have heard in the news about influenza and a possible flu pandemic. Hand out the student sheets and have students observe and describe the virus diagram in step 1 (*e.g., like a golf ball with a coating and spikes, like a solid mass with a sack around it, like a circle with a rim with points*). After students share their descriptions, make a two-column chart that relates their analogs to specific names and features of an influenza A virus. Tell students that one way avian and human influenza A differs is in the cells the viruses can easily infect. Avian infects bird cells; human infects human respiratory tract cells. Infection is determined, in part, by the glycoprotiens.
3. Have partners complete step 2, matching the influenza replication steps. Review as a class.

4 Divide the class into teams and have them do Part 2, the *Making an Influenza Virus Hybrid* activity. Remind students that the two labeled paper clips code for the H and N surface glycoproteins. Have teams tally the number of viral hybrids that have one or two avain surface glycoproteins. Record in a table on the board.

5 Have students answer the questions at the end of the activity. Review the activity by discussing the activity sheet questions and questions such as: Why might the reassortment process result in viruses that may not be initially recognized by our immune system? (*A whole strand of RNA was exchanged in one cycle of replication, so a large part of the protein could change. If this protein is new to the immune system, it may not recognize it. Thus, it may not act quickly to control the virus, making the infection potentially deadly.*)

Answer Key to Step 2: Influenza A Viral Replication (contains more information than student sheet):
1 (f); 2 (j); 3 (a); 4 (h); 5 (b); 6 (d); 7 (i); 8 (g); 9 (c); 10 (e)

1 The glycoprotein spikes on the surface of a virus are like keys that fit a lock. In the case of a host cell, the lock is called a cell receptor. When this lock and key bond, the virus can enter or exit the cell. The H spikes help a virus enter a cell, and the N spikes help it leave.
2 The virus enters the cell (endocytosis).
3 The virus loses its envelope in the cytoplasm, and the remaining viral core moves to the nucleus. (Many other kinds of viruses stay in the cytoplasm and never enter the nucleus.)
4 The virus is transcribed in the nucleus. (Viral RNA must be transcribed to + sense mRNA strands before being translated to protein.)
5 Viral proteins are made in the cytoplasm using the host cell's ribosomes.
6 Some of these viral proteins move to the nucleus to aid in viral replication. The virus replicates (makes viral RNA) in the nucleus. (Replication involves copying original – sense strand RNA to + sense strand RNA and then back to new– sense strand viral RNA.)
7 Other viral proteins move to the nucleus and aid in virus assembly.
8 Some proteins become glycoproteins, such as HA and NA, move to the host cell's membrane.
9 The viral core moves from the nucleus to the cell membrane. At the cell membrane, the viral core is enveloped in a lipid coat that has viral H and N glycoproteins on its surface.
10 The new virus exits the host cell, ready to infect another cell or to infect someone else if the infected person coughs it out.

Answers to Questions on Student Handout:

1 Name one way avian and human influenza A viruses are alike and one way they are different. *Alike: They are both influenza A, and both can be deadly. Different: They typically infect different organisms, partly because of their surface glycoprotiens. Humans spread influenza A by coughing and sneezing; birds spread it through feces.*

2 Why might hybrid viruses be potentially deadly to humans?
Most human immune systems do not quickly recognize and respond to these viruses. Because the virus has RNA from the human strain, it may be able to spread easily from person to person. This combination of factors may make this hybrid virus potentially very deadly.

3 Name three behaviors that could prevent the spread of human influenza A.
Covering one's mouth when coughing or sneezing; washing hands; getting vaccinated; washing surfaces; not touching surfaces that are commonly used; and staying home when sick with the flu.

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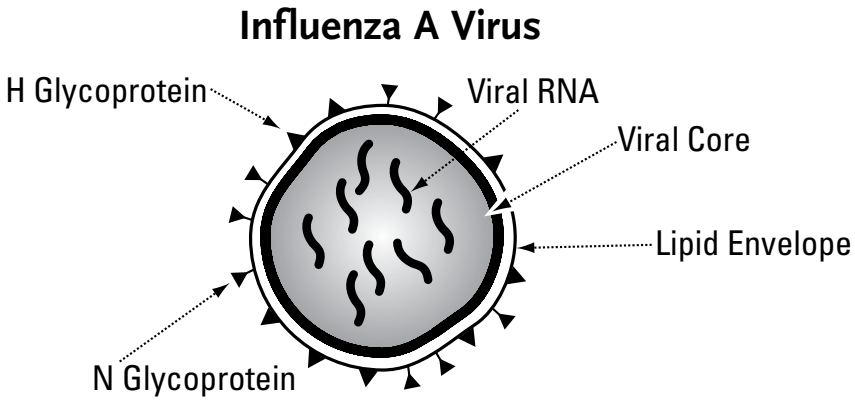
Modeling an Avian-Human Hybrid Flu Virus

What is an influenza virus? How does it replicate in cells? In this activity, you will make virus models and use them to examine how avian and human influenza A viruses can mix in the same cell to generate a potentially more dangerous virus.

PART 1: HOW THE INFLUENZA A VIRUS REPLICATES IN A CELL

1 Examine the virus diagram and describe it in everyday terms or by using an analogy. For example, it looks like a pin cushion or a circle with nails sticking out.



Write your analogy on the lines below.

GLOSSARY

- **Endocytosis**: The process by which some kinds of viruses are surrounded by the host's cell membrane and taken into the cell.
- **Hemagglutinin** (HA or H): A glycoprotein (protein with an attached sugar group) on the surface of an influenza A virus that helps it enter a host cell.
- **Neuraminidase** (NA or N): a glycoprotein on the surface of an influenza A virus that helps it exit a host cell.
- **Host cell**: The cell infected by a virus.
- **Replication**: Copying of influenza A RNA strands.
- **Transcribed:** RNA copied to a form that can be translated to proteins at host cell ribosomes.
- **Viral core**: Contains influenza's RNA strands and important proteins.
- **Viral envelope**: A viral covering not present on all viruses. It is made from the membrane of the host cell and sometimes has viral spikes.
- **Virus:** an infectious agent that has DNA or RNA and a protective covering. It relies on the host cell to replicate.

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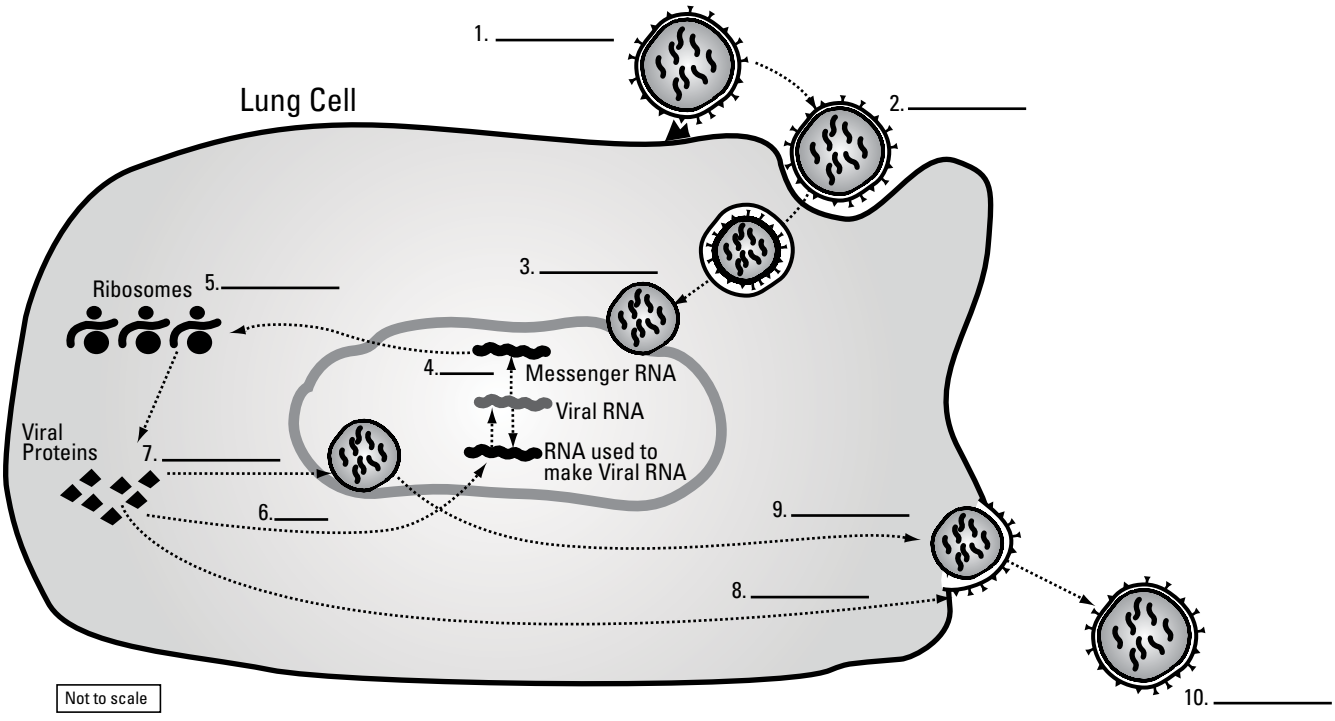
2 Study the influenza A replication diagram below and read the descriptions, labeled A–J, describing the replication process. The order of these steps is scrambled. Match each description below to its appropriate replication step by writing the step's letter on the correct line.

Influenza A Viral Replication in a Lung Cell



a) The virus loses its envelope in the cytoplasm, and the remaining core moves to the nucleus.

b) Viral proteins are made in the cytoplasm using the host cell's ribosomes.

c) The viral core moves from the nucleus to the host's cell membrane. At the cell membrane, the viral core is enveloped in a lipid coat that has viral H and N glycoproteins on its surface.

d) Some viral proteins made in the cytoplasm move to the nucleus where they aid in viral replication. The virus replicates in the nucleus.

e) The new virus exits the host cell, ready to infect another cell or another person if it is coughed out by the infected person.

f) The glycoprotein on the virus attaches to the cell plasma membrane.

g) Some proteins become glycoproteins (H and N) and move to the host cell's membrane.

h) The virus RNA is transcribed to messenger RNA in the nucleus.

i) Some viral proteins from the cytoplasm move to the nucleus and aid in virus assembly.

j) The virus enters the cell (endocytosis).

PART 2: MAKE AN INFLUENZA A HYBRID VIRUS MODEL

Learn how influenza A RNA can reassort when a cell is infected with an avian and a human influenza virus. The concern is that such an influenza A viral hybrid could lead to a flu pandemic.

Materials and Lung Cell and Viral Parts They Represent:

Common Object	Cell and Virus Parts Represented by Object
quart-size plastic bag	lung cell plasma membrane
pint-size plastic bag	lung cell nuclear membrane
2 plastic eggs	Influenza A viral envelopes
8 paper clips (two with labels) and 2 small rubber bands, all of one color	8 strands of viral RNA (human or avian), 2 labeled clips code for surface glycoproteins; rubber bands for surface glycoproteins
8 paper clips (two with labels) and 2 small rubber bands, all of the same color but a different color from the set above	8 strands of viral RNA (human or avian), 2 labeled clips code for surface glycoproteins; rubber bands for surface glycoproteins
2 film containers	outer protein part of viral core

1. Referring to the table above and the diagrams:
   - Make a lung cell with a nucleus.
   - Assemble one avian influenza A virus and one human influenza A virus.
2. Infect the lung cell with the avian influenza A virus by following steps 1–3 in Part 1 of this lesson. Repeat with the human influenza A virus.
3. Mix the RNA strands from the two viruses. Without looking, remove eight RNA strands from the nucleus. Make sure two of the eight strands have labels.
4. Put the RNA in a film container (core). Insert the core into a plastic egg (viral envelope) to make a new virus that could potentially infect another cell. Use the rubber bands that match the labeled paper clip colors to make surface glycoproteins on the envelope of your hybrid virus model. To make the surface proteins three-dimensional, close the egg on the bands so they stick out from the side of the egg. Does your virus model have any surface proteins from the avian virus? Tally these in a chart on the board.

Questions

1. Name one way avian and human influenza A viruses are alike and one way they are different.

_____

2. Why might hybrid viruses be potentially deadly to humans?

_____

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3. Name three behaviors that could prevent the spread of human influenza A.

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GLOSSARY

- **H5N1**: A strain of avian influenza A that usually kills poultry, but often doesn't kill wild birds. Humans are rarely infected by this virus, but when they are, the virus is often deadly.
- **Influenza A**: A group or type of influenza that infects animals and humans
- **Pandemic**: A global infectious disease outbreak
- **Reassortment**: The process by which RNA strands from two or more different influenza viruses mix and result in hybrid viruses.