Rationale: Students will learn about the virus infection cycle, and the role that sialic acids and viral proteins play in the process. In addition, the relationship between inflammation and flu symptoms and the use of flu drugs and flu vaccines will be reviewed. Students will learn these concepts by watching videos and answering associated questions.

Background Information:
Researchers in the Wakarchuk laboratory at Ryerson University are working with *E. coli* to engineer it to complete human-like glycosylation functions on human therapeutic proteins. Glycosylation is the most prevalent and diverse protein modification that occurs in humans, with 70% of human proteins being glycosylated. Glycosylation is the addition of a carbohydrate unit or chain to a protein. Sialylation is a type of glycosylation that involves the addition of sialic acid, a type of sugar, to proteins. The addition of sugars, and in particular sialic acid, to therapeutic proteins will reduce side effects and increase the circulatory half-life of therapeutic proteins in patients.

After obtaining a greater understanding of glycosylation and sialylation, the desire to relate it to high school science concepts became a priority. Sialic acid on human host cells acts as a receptor for the influenza virus. Many textbooks state that the influenza virus simply attaches to a host human cell, but fail to mention the role that sialic acid plays in this attachment. This website allows for a greater understanding of the influenza virus infection cycle, including the role of sialic acid and viral proteins. In addition, symptoms of the flu due to inflammation, the use of flu drugs and flu vaccines are also discussed. These topics relate to the Diversity of Living Things unit of the Grade 11 University Preparation Biology course, and to the Microbiology unit of the Grade 11 College Preparation Biology course.

Curriculum Connections:

**Grade 11 University Preparation Biology**
- B2.1 use appropriate terminology related to biodiversity, including, but not limited to: genetic diversity, species diversity, structural diversity, protists, bacteria, fungi, binomial nomenclature, and morphology
- B3.2 compare and contrast the structure and function of different types of prokaryotes, eukaryotes, and viruses (e.g., compare and contrast genetic material, metabolism, organelles, and other cell parts)
<table>
<thead>
<tr>
<th>Grade 11 College Preparation Biology</th>
</tr>
</thead>
<tbody>
<tr>
<td>• C3. demonstrate an understanding of the diversity of microorganisms and the relationships that exist between them</td>
</tr>
<tr>
<td>• C2.1 use appropriate terminology related to microbiology, including, but not limited to: fission, conjugation, phage, dormancy, morphology, mycelium, spore, pathogen, and plasmid</td>
</tr>
<tr>
<td>• C3.4 explain the different methods of reproduction in various types of bacteria, viruses, and fungi</td>
</tr>
<tr>
<td>• C3.5 describe how different viruses, bacteria, and fungi can affect host organisms, and how those effects are normally treated or prevented (e.g., hepatitis viruses can damage the liver, but vaccinations can prevent infections; streptococcus bacteria can cause respiratory infections, which are treated with antibiotics; ringworm is a fungal infection of the skin, treated with fungicides)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesson Objectives/Concepts:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Students are responsible for learning several concepts on their own before they are taught/reviewed in class</td>
</tr>
<tr>
<td>• Students will learn about the influenza virus infection cycle and the role that sialic acid and viral proteins play in the process</td>
</tr>
<tr>
<td>• Students will learn the connection between inflammation and certain flu symptoms</td>
</tr>
<tr>
<td>• Students will learn about available flu drugs and flu vaccines and how they work</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Materials: Access to the Internet, student handout, chart paper, overhead projector, blackboard.</th>
<th>Time: 1.2 periods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A period is 75 minutes.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Introduction (10 minutes):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questions to ask the class:</td>
</tr>
<tr>
<td>1. Briefly describe the influenza virus infection cycle in your own words.</td>
</tr>
<tr>
<td>2. What is sialic acid?</td>
</tr>
<tr>
<td>3. What are some important viral proteins involved in the influenza virus infection cycle?</td>
</tr>
<tr>
<td>4. What are some flu drugs and flu vaccines available on the market?</td>
</tr>
<tr>
<td>The answers to these questions will give the teacher an idea of the readiness level of the class.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Activities/Procedure (60 minutes):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-teaching, done in advance of this lesson:</td>
</tr>
<tr>
<td>• Ensure you have taught students the basic structure of viruses (genetic material surrounded by a protein coat) and the fact that viruses are not part of any of the kingdoms due to their inability to reproduce independently from a host, the fact that they do not make or use energy, and they do not produce waste.</td>
</tr>
</tbody>
</table>
| • Ensure you have given students a couple of days to visit the website and answer the
video associated questions.

**Lesson:**
- Students should be divided into small groups. Each group is responsible for one topic that the website covers. Depending on the size of the class, the division of topics will vary. Groups of students should work together to go over the topic they have been assigned until they are comfortable explaining it. Using chart paper, an overhead projector or the blackboard, each group is to teach the class their part. Depending on the division of topics, the amount of time allotted to each group will vary.
- Groups are to take up the questions associated with their topic (video) with the class.
- The teacher should circulate around the room guiding students as necessary, and answering any questions that come up as students prepare their lesson.

**Summary/Closure (20 minutes):**
- The teacher should review the key concepts that were learned from the website with the class.

**Assessment:**
- As you are circulating around the classroom, assess the level of understanding amongst the groups of students.
- You may collect student answers to video associated questions to assess them for accuracy.
- Answers to website video questions are provided.

**Extensions/Connections:**
- With some modifications, this exercise can be more formalized, with students being evaluated for their teaching. However, since this may be the first time that students are expected to learn several concepts on their own, this lesson does not include a rubric. This lesson is intended as an opportunity for students to be more independent learners, to work together and to practice their communication skills.
Answers to video questions:

**Video 1: When Flu Viruses Attack!**

1. How many pieces of RNA are in the influenza virus?
   - 8

2. What flu virus protein was drawn as a hand in the video? What does it do?
   - Hemagglutinin; it holds/attaches onto sialic acid

3. What flu virus protein was drawn as a pair of scissors in the video? What does it do?
   - Neuraminidase; it nicks/cuts sialic acid

4. As human cells start dying/get damaged, cell contents start leaking out. What does this cause?
   - Inflammation

5. When the immune system initiates a strong response to fighting the flu virus, constitutional symptoms occur. What are these?
   - Fever, chills, fatigue, body aches

6. Respiratory symptoms are partially explained by inflammation. What symptoms are present if inflammation is located in:
   - The nose?
     - Stuffy or runny nose
   - The throat?
     - Sore throat
   - The lungs?
     - Cough

**Video 2: Influenza Virus Infection – Carolyn Bertozzi**

1. How many deaths occurred in the 1918 flu pandemic?
   - 70 million

2. What 2 groups of people can the flu be very deadly for?
   - The elderly and very small children

3. What are 2 organisms other than humans that the flu can infect?
   - Birds and Pigs (swine)
4. When did scientists start figuring out that the very early stages of viral infection involve sugars?
   • 1970s and 1980s

5. What do the letters in the swine flu strain H1N1 stand for?
   • H1-hemagglutinin form 1
   • N1-neuraminidase form 1

6. Create a flow chart showing the steps in the lifecycle of an influenza virus.

   Hemagglutinin holds/attaches onto sialic acid
   ↓
   Virus can now dock onto the cell surface
   ↓
   An endocytosis event is triggered and the virus is engulfed by the host cell into a vesicle
   ↓
   Viral and vesicle membranes fuse and the virus releases nucleic acid (RNA) into the cell
   ↓
   Viral nucleic acid takes over host cell’s machinery and forces the cell to make virus particles
   ↓
   Virus particles assemble around the host cell membrane
   ↓
   Viral particle buds from host cell’s surface
   ↓
   Neuraminidase nicks/cuts sialic acid so virus can release itself and find another cell to infect

7. Name 2 flu drugs that are neuraminidase inhibitors. How are they able to act as inhibitors?
   • Relenza and Tamiflu; they look like sialic acid (its transition state)

**Video 3: Flu Vaccine Risks and Benefits**

1. How is a TIV vaccine administered? What form is the virus in?
   • By injection; it’s dead

2. How is a LAIV vaccine administered? What form is the virus in?
   • By nasal spray; it’s live (alive) but weak

3. What are 2 uncommon but serious risks of the flu vaccine?
   • Guillain-Barré Syndrome (a nerve disease that causes muscle weakness) and Febrile seizures
4. What is the efficacy of the flu vaccine?
   • 60-70%

5. In the United States, how many hospitalizations and how many deaths does the flu cause?
   • 200,000 hospitalizations and 3,000-49,000 deaths per year

6. What illnesses are responsible for the deaths of people with the flu?
   • Pneumonia
   • Bronchitis
   • Asthma
   • Ear infections
   • Sinus infections
   • Bacterial infections

7. What are 2 myths of taking the flu vaccine?
   • That the flu vaccine causes autism (due to the thimerosal/mercury preservative)
   • That having too many vaccines is bad for the immune system

8. What is herd immunity?
   • When many people are immune (i.e. by vaccination), it helps prevent vulnerable people from getting ill (ex. 3-month-old baby that is too young to be vaccinated)