## Teaching Notes

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**Course Information**

Department: Biology, Bradley University

Level: **Lower – parts for freshman biology (parts 1-3), parts for upper level genetics (4-6)**

Course type: **Both (this case could be used for either a lecture or lab course)**

Students: **Majors**

Number of Students: 15 students at Bradley (also used elsewhere)

**Module Information**

Original Module Name: **Understanding COVID-19 Biology to Design a Vaccine**

Link to Original:

[Adapted Module Name: (if applicable)

Link to Adapted Module]

Modified Module Name:

Files associated: Worksheets and supplemental documents

Learning Goals:

* Develop an understanding of viral infection and possible treatments
* Utilize the knowledge available in protein sequence to understand infection (attachment) and host cell specificity
* Develop bioinformatic and protein visualization skills using freely available software to explore protein structure and function

**Teaching Notes**

**Introduction**

The case presented here is written during the COVID-19 pandemic (Spring 2020) and uses this backdrop to introduce students to the initial stages of developing a vaccine against the SARS-CoV-2 virus, targeting its spike (S) glycoprotein. The viral protein binds to a specific human protein on human epithelial cells and this initiates the infection. The structure of the viral spike and human receptor protein interaction was determined using cryo-electron microscopy by Yan *et al* (2020). Using the freely available molecular structural data and publicly available visualization software and bioinformatics tools and resources, the case leads students to examine the interaction of the viral spike (S) protein with the human epithelial cell ACE-2 protein, the site of viral attachment. The vaccine development discussed in this case is focused on blocking this interaction to stop infection.

Parts of the case could be delivered to different levels of students in a flipped class or worksheet manner. The first two worksheets are suitable for all levels of biology. There is a supplemental ethics question for worksheet 2 regarding the use of off-label drugs or unapproved technologies in this pandemic. Additional reading that can be assigned is listed in the resources section.

The third and fourth worksheets may be more suited to genetics or biochemistry students as these worksheets involve an introduction to using molecular visualization software (iCn3D) and analysis of a paper that discusses the protein-protein interaction of the SARS-CoV-2 S protein with the human ACE-2 transmembrane protein. Students also learn to query the sequence databases to find and compare the amino acid sequences of viral and host proteins involved in the infection. Worksheet 5 is an assessment of the skills presented in Worksheet 4 that allows students to use the bioinformatics skills and understanding of the Yan *et al* (2020) paper to make further predictions about the structures involved.

**Target audience**

The case is targeted for introductory biology students (worksheets 1 and 2) at the high school or college/university level. The additional worksheets could be used in a genetics or biochemistry course. The bioethics supplemental portion could be used for all levels of students.

**Prerequisite knowledge**

Worksheet 1 - COVID-19 Pandemic

Students are introduced to the cause of the pandemic and basic viral biology. Students should read or have been introduced to basic viral terminology. Recommended reading is an introductory biology textbook or [OpenStax Biology2e Chapter 21](https://openstax.org/books/biology-2e/pages/21-introduction) (introduction through section 21.3). Additional open source material may be found in [OpenStax Microbiology](https://openstax.org/books/microbiology/pages/6-1-viruses).

Worksheet 2 - Finding a treatment

Students should understand the basics of the central dogma in terms of the use of an mRNA for a vaccine.

Worksheets 3-4 and assessment

These worksheets use freely available bioinformatics tools to explore the protein structure (worksheet 3) and the sequence comparison of the viral S protein (worksheet 4) and the ACE-2 protein (assessment). Students should have an understanding of chemical bonds that are important in protein-protein interaction. The assessment piece is an extension of worksheets 3 and 4 to build on students' knowledge of the interaction and skills in performing bioinformatics searches.

**Classroom management**

This case has been designed to be used in a flipped classroom or as a worksheet assignment for students to perform outside of in-class time. The first two parts are not technical and can be used as short assignments, the bioinformatics portions may take more time for less experienced students.

**Blocks of analysis**

Worksheet 1 - this worksheet introduces students to basic virology and the COVID-19 pandemic through data, videos and podcasts. Time estimate is 30-60 min.

Worksheet 2 - through videos and images, students are provided basic information regarding approaches to treating the COVID-19 outbreak in short-term and long-term manners. No known methods of treatment are currently available (spring 2020), but many different approaches are being explored. Students can further explore other treatments through the resources included in the Millikin link as well as DrugBank. Time estimate is 1-2 h.

Worksheet 3 - this worksheet first leads students to visualize the protein-protein interaction of the SARS-CoV-2 S protein with the ACE-2 protein (attachment of the virus to epithelial cells). The students use the structural data from (PDB entry 6M17) to visualize the structure deposited by Yan *et al*, 2020. In the second part of this worksheet, students are encouraged to explore the images from Yan *et al*. (2020) to see the interaction. More advanced students should be encouraged to try and recreate these figures using iCn3d. Time estimate is 2 h for first time users.

Worksheet 4 - students explore the sequence similarity between S proteins from various coronaviruses and locate amino acids identified by Yan *et al*. (2020) as important for the SARS-CoV-2 S protein interacting with the ACE-2 protein. Time estimate is 2 h for first time users.

Assessment (worksheet 5) - this optional assessment asks students to generate a multiple sequence alignment of the ACE-2 protein from various species and to use the information from Yan *et al*. (2020) to look for residues that may be important in the interaction. Time estimate is < 1 h.

**References**

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