Instructor information

Is antibody X likely to provide protection against SAS-CoV-2?

In this project, students investigate the effects of mutations on the ability of a commercial antibody to bind to the SARS-CoV-2 spike protein. If a SARS-CoV-2 variant develops mutations that prevent binding, that variant will be more likely to escape from antibodies to earlier forms of the spike protein and some commercial antibodies will be no longer be effective.

This project contains five parts. Each part is accompanied by a sheet for recording data. Students are advised to scan the data sheets before starting a part so they know what information to capture.

Advise students to read and follow the directions slowly and carefully. Capitalization and spelling matter. If they run into trouble, have them go back a few steps and make sure all the correct options are selected.

This research project includes:

1. The changing shapes of the SARS-CoV-2 spike protein (*optional*).

This activity involves comparing structures with different conformations of the SARS-CoV-2 spike protein and can be used as an introduction.

Estimated time: 1-2 hours

1. Finding and viewing aligned structures (*optional*).

This protocol can be used to find structures, align structures by shape, and alternate between the aligned structures. Aligning structures 6M0J and 6XE1 shows where the antibody in 6XE1 binds to the spike protein and where ACE2 binds to the spike protein. Alternating between the structures demonstrates how some antibodies can block binding to ACE2 and prevent SARS-CoV-2 from infecting a cell.

Estimated time: 1-2 hours

1. Identifying amino acid contacts (*optional*).

This protocol shows how to use iCn3D to select amino acids within a certain distance of another molecule. If amino acids are close to other atoms (within 4 angstroms), they are likely to be important in binding.

Estimated time: 1-2 hours

1. Look at the emergence of variants in NextStrain.org and find a protein sequence.

Students use NextStrain.org to find a variant to investigate, then find the protein sequence for the spike protein from that variant. This protein sequence is used in the last step of the project.

Estimated time: 1-2 hours

1. How does the spike protein help SARS-CoV-2 hide from the immune system and infect cells?

Students work in iCn3D to align the protein sequence of the variant to the protein sequence of a spike protein, in a structure that contains at least one antibody. Next, students highlight the antibody binding site and identify amino acids that are mutated in the variant. Last, students compare the bonds formed by the normal and variant amino acids and use that data to predict or explain the effect of that mutation on antibody binding.

Estimated time: 1-2 hours

1. Commercial Anti-SARS Antibodies: a spread sheet with commercial antibodies and their corresponding PDB structures.
2. CDC info 5\_3\_2022: A spread sheet, with data from the FDA, showing the status of several commercial antibodies as of early May 2022.

The first three parts of the project are optional. These involve comparing different spike protein structures, learning how to use VAST+ and the NCBI to find aligned structures, and learning how to annotate information in iCn3D and identify binding sites.

Parts 2 and 3 can include a research component by having students find their own aligned antibody structures (part 2) and identify the binding sites for those antibodies (step 3). You may even want to compile data from multiple students to show how different antibodies bind to different parts of the spike protein receptor binding domain.

The main research component is carried out in parts 4 and 5. In part 4, students find their own emerging variant to investigate and obtain the spike protein sequence from the NCBI.

In part 5, students are assigned an antibody to investigate by the instructor. Information about the antibodies is found in two spread sheets: Commercial Anti-SARS Antibodies and CDC info 5\_3\_2022.

Use the Commercial Anti-SARS Antibodies spreadsheet to find antibodies for students to investigate. Provide students with the name of the antibody, the PDB ID for the structure, and the name of the drug. Do note that some structures contain two antibodies. Be sure students are able to determine which antibody is the one you want them to investigate.

Do *not* use Ly-CoV555, officially named Bamlanavimab since this one is used as an example in the assignment. Of the others, there are nine different antibodies that students can investigate. Since each student is likely to find a different variant in NextStrain.org, combining the antibodies with protein sequences from emerging variants creates a large number of samples whose results are unknown.

Some structures are included in the table that contain sequences from an Omicron variant. You may wish to extend this project by having students use these structures to test the predictions they made in part 5 by modeling the mutations.

You can use the CDC info 5\_3\_2022 spreadsheet to see which antibodies continue to be used.