The changing shapes of the SARS-CoV-2 spike protein

The SARS-CoV-2 spike protein has a special domain that changes shape (conformation). In the closed conformation, this domain is hidden from the immune system. In the open conformation, this domain can stick out and bind to a receptor on the surface of a cell. This domain is known as the receptor binding domain (RBD) because of its ability to bind to the receptor for SARS-CoV-2.

Comparing structures of the spike protein in the open and closed conformations shows how one conformation helps the receptor binding domain hide from the immune system and the other conformation allows the receptor binding domain to contact a receptor and start infecting a cell.

Identify a shape change in the SARS-CoV-2 spike protein and the locate the Receptor Binding Domain

1. Find a structure with the SARS-CoV-2 spike protein in the closed conformation and open it in iCn3D.
   1. Go to the National Center for Biotechnology Information ([NCBI](file:///Users/sandy%201/Documents/Antibody%20engineering/Hackathon%20Jan%202022/SARS%20CoV2%20vs%20antibodies/NCBI)) (https://ncbi.nlm.nih.gov).
   2. Search for 6VXX.
   3. Click the full-featured 3D viewer button in the structure window to open the structure in iCn3D.
   4. Turn the structure around and look at the three protein chains. These are identical subunits of the spike protein. One, two, or three of the spike protein chains can be found in an open conformation or a closed conformation.
2. Align the structure to a spike protein structure with at least one protein chain in the open conformation.
   1. Click the File button and choose Align > Structure to Structure > 2 PDB structures.

Graphical user interface, text, application

Description automatically generated

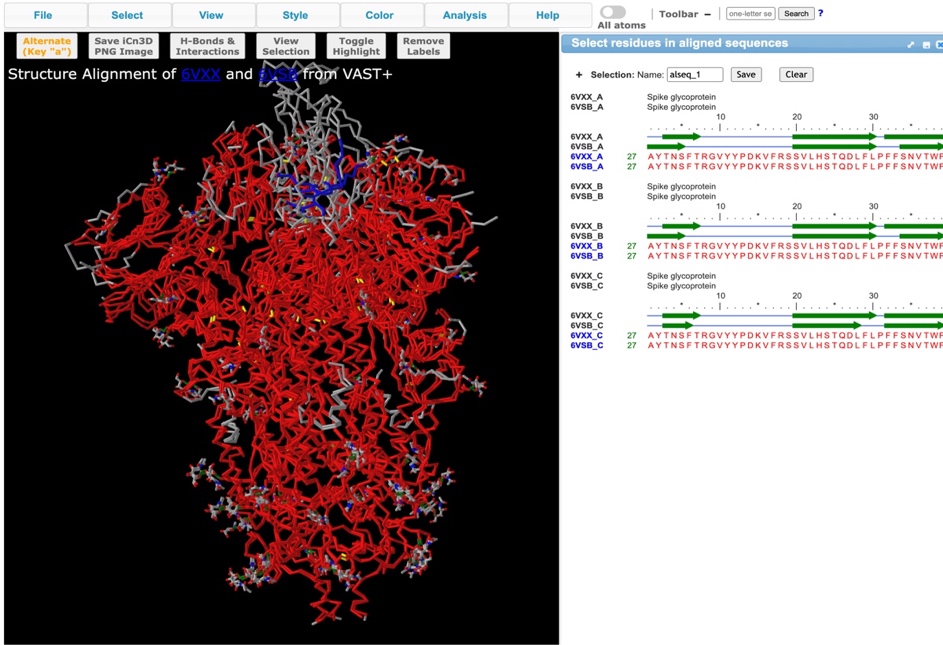
* 1. Enter PDB IDs 6VXX and 6VSB in the fields for ID1 and ID2 and click All Matching Molecules Superposed. 6VSB has one chain in the open conformation.

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* 1. Look for regions of the proteins that are aligned and regions that are not aligned.

When the structures appear, the parts of the protein chains that are similar enough to be aligned will be shown in red. The unaligned regions will be shown in grey and blue.



1. Compare the two structures and identify the receptor binding domain (RBD).
   1. Turn the structures so that the largest unaligned grey region appears at the top.
   2. Press the “A” key on your keyboard or click the button that says “Alternate” to alternate between structures 6VXX and 6VSB. You’ll have to press it more than once.

You should see the shape of the unaligned grey region change, from pointing downward into the center of the spike molecule, to pointing upward. You can turn the structure around to see it better.

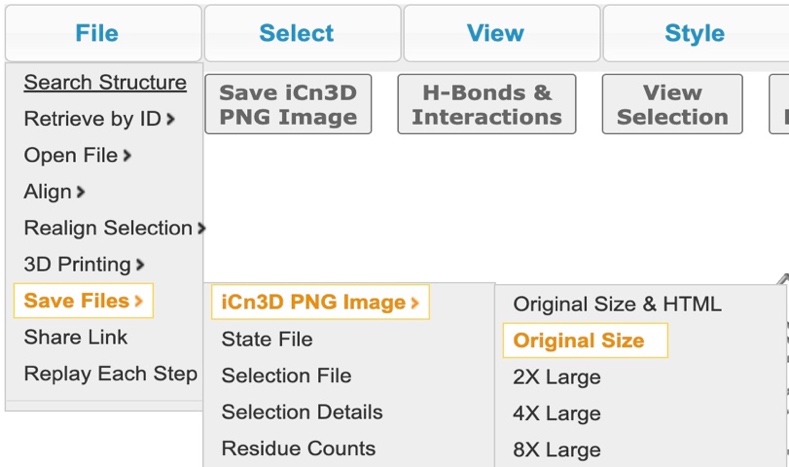
That grey region is part of the Receptor Binding Domain (RBD).

* 1. Alternate between the structures until you have the receptor binding domain pointing up.
  2. Open the Style menu. Change the background color by choosing Background, White.

A picture containing graphical user interface

Description automatically generated

* 1. Save an iCn3D PNG image for each of the two structures. You should one image that shows the spike protein in a closed position and one that shows the spike protein in an open position.



* 1. Paste the image files (png) in a document to hand in.
  2. Circle the receptor binding domain in an image showing the open conformation. The spike protein only binds to its receptor in the open conformation.