Antibody: Flexible Form and Function

Learning Objectives

Learning objectives were adapted from Suchman *et al.* 2018.

1. **Describe** how antigens and epitopes are related using examples of virus antigens.
2. **Explain** why some antibodies that do not bind to epitopes are produced.

Alignment with North Carolina Science Standards

- Middle Grades 6-8 (source: PDF)
  - **Bio.4.1 Understand how biological molecules are essential to the survival of living organisms**
    - Bio.4.1.1 Compare the structures and functions of the major biological molecules (carbohydrates, proteins, lipids, and nucleic acids) as related to the survival of living organisms.
- High School Biology PDF
  - **Bio.4.1 Understand how biological molecules are essential to the survival of living organisms**
    - Bio.4.1.1 Compare the structures and functions of the major biological molecules (carbohydrates, proteins, lipids, and nucleic acids) as related to the survival of living organisms.

Identify and describe alignment:

- Students will compare the structures of a major biological molecule category, proteins, using 3D printed models and relating their shapes to their functions. Specifically, students will connect the structure of an antibody (protein) to its capability to detect a pathogen (protein) and elicit an adaptive immune response for organismal survival.

Instructor Information

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Models

Pre-Files for 3D Models

STL files to print the influenza virus and antibody models were obtained from the Suchman *et al.* 2018 publication and can be accessed for printing at Thingiverse. STL files to print the SARS-CoV2 models were obtained from Thingiverse (COVID-19-top.STL file included as part of the COVID-19 Bobble Virus).

Printing and Adapting Antibodies

The NSF STEM BUILD program adapted the models and printed them at the NC State University Libraries Makerspace. Influenza virus and SARS-CoV2 models were printed using 2.85-mm PLA filament. Heavy chains and light chains were printed using 2.85-mm TPU flexible filament. Magnets were glued to heavy and light chains to allow different combinations to be used to create antibody molecules. We appreciate the time Vianey Ramirez spent printing and improving the models.

Activity Description and Resources

Participants access the website: go.ncsu.edu/antibody and watch the 3-minute video Antigens & Antibodies to learn about them and how they are related to human health and virus infections. Next, participants begin with the first part of the activity in the Handout (labeling). During the synchronous session, students will work with the models to address the interactions, making connections with the biological functions.

Activities

Pre-session Activities

Students receive the models and a link to the website with instructions to watch two overview videos with captions and complete the first activities described on the website.

Students watch short videos on the immune system and antibodies and vaccines at home before coming to the flipped session. The mini-lecture video is 3.5 minutes long. The videos are available on YouTube and are posted on the Intro page of the activity website. The labeling activities to be completed before the synchronous session are included in the Handout.

Synchronous Activities

Students

1. Instructors screen share Antibody Activity Slides via Zoom throughout the activity.
2. After introductions and a review of what an antibody is (slide 3), students and instructors review the questions that were asked in the pre-activity parts of the Handout.
    a. Students are asked to label the heavy and light chains, variable regions, constant regions, and the region of the antibody that binds an epitope. They are given a link to a Jamboard to do this. This could also be done by collectively annotating a Google Slide, annotating in Zoom, or on paper. Answers are reviewed on slide 5.
    b. Students are asked to determine how many different types of epitopes exist in the diagram of a viral particle (slide 6), and the group discusses the relationship between epitopes, antigens, and antibodies.
3. Students are next asked to begin to explore the Tactile Teaching Tools. This exploration is structured with a series of multiple choice questions, which could be structured as Zoom polls, on paper, or using a classroom response system.
    a. How many viral spike types (epitopes) can you identify?
        i. Four distinct epitopes are present. Students might correctly state that there are actually more epitopes, as different sides/faces of each structure might be able to bind different antibodies.
    b. The 3D antibodies are composed of…
        i. White heavy chains and blue light chains.
    c. Which epitope does the antibody formed from heavy chain 1 and light chain 1 bind?
        i. Four epitopes are labeled A-D on a photo of the influenza virus TTT. The antibody has a small binding pocket that can only bind epitope D (the “spike”).
        ii. A 30-second video shows one of the instructors testing Antibody 1’s ability to bind to the different epitopes.
    d. Which epitope does the antibody formed from heavy chain 2 and light chain 2 bind?
        i. Four epitopes are labeled A-D on a photo of the influenza virus TTT. The antibody has a large, spherical binding pocket that binds epitope C (the “ball”). Students might also state that the antibody is able to bind to some of the other epitopes, which can lead to a discussion about the strength of binding: other epitopes, such as the spike, can fit within the binding pocket, but this leaves a large amount of empty space within the binding pocket.

        ii. A 30-second video shows one of the instructors testing Antibody 2's ability to bind to the different epitopes.
    e. The students are instructed to create new antibodies by attaching light chain 1 to heavy chain 2, and vice versa. Do the new antibodies bind the epitopes?
        i. They bind more weakly. The group may discuss here the fact that many other heavy and light chains exist beyond these two, and it is possible that there are other combinations that would bind better.
    f. The students are instructed to reassemble the original two antibodies and to attempt to bind them to epitopes on the SARS-CoV2 TTT. Do either of the original heavy/light chain combinations bind to antigens on the coronavirus?
        i. No. The group may discuss what this tells us about antibody specificity.
4. Slide 17 contains a series of discussion questions aimed at contextualizing the concepts the students learned through their interactions with the TTTs.
    a. Do all antibodies share the same binding region?
    b. When an antibody binds to a virus, is it able to recognize every epitope presented by the virus?
    c. Why is binding of an antibody to bind to an epitope important in the immune response?
    d. What does vaccination have to do with the production of antibodies?
5. Slides 18 and 19 explain how vaccines work, and how antibodies generated in response to a vaccine or a natural infection protect the body from the pathogen.
6. Slide 20 provides examples of detailed molecular structures of a viral particle and an antibody.

Website https://go.ncsu.edu/antibody

References:

Suchman E.L. *et.al.* (2018). Modeling Antibody-Epitope Interactions with 3D Printed Kits in Large or Small Lecture Courses. HAPS Educator 22 (1): 73-78. doi: 10.21692/haps.2018.009