# Exploring proteins of the immune system

## *How might we identify an unknown protein from an amino acid sequence and predict its three-dimensional shape?*

The human body must protect itself against environmental threats, including many microorganisms, parasites, and hazardous substances. To accomplish this, the human **immune system** is like a built-in security system that defends our bodies from invaders. The invaders may include pathogens such as bacteria, viruses, or fungi. The act of defense or **immunity** is highly structured, consisting of a complex network of specialized cells, cellular components, and associated proteins. As with much of science, the organization and classification of components within human immunity change as new information is gained by research using the latest tools. The classic view of the human body's defense is that components fall within two categories: *innate* and *acquired immunity.*

Complete the following activity using various amino acid sequences.

*A pharmaceutical company is studying a new immune response triggered by an unknown protein, found in a sample from a patient who recovered quickly from an infection. The company needs your help to figure out what this protein is and what role it might play in immunity.*

- Use BLAST to search for matches and identify the likely name or family of the protein.
- Explore UniProt to investigate its known functions, where it's expressed, and any roles it might play in the immune system.
- Use AlphaFold to visualize the protein's 3D shape and think about how its structure might help it carry out its function.

## Materials

- Amino acid sequences: ***ols.plus/uniprot***
- Computer with internet connection

## Procedure

1. Copy your assigned amino acid sequence.
2. Visit ***uniprot.org/blast***.
3. Paste your assigned immunological protein sequence into the larger text box.
4. Name your BLAST job. Keep all default settings in drop down boxes.
5. Click the blue "Run BLAST" in the lower right side of the page.
6. Wait for BLAST analysis to finish, then click on 'Completed' to view results.
7. Look at the Overview tab.
8. In the Overview table, find the top record (first row) and fill in the information below:

- Entry number _____
- Entry name _____
- Protein name _____
- Gene name _____
- Organism _____
- Length (amino acid) _____

9. Explore the protein page by clicking on the blue Entry Number.
10. Write 1–2 sentences describing the protein's function. Note: There will be a lot of immunological words you may not know on this page. Try your best to pick 1 or 2 functions, and if needed, try to define difficult terms using alternative sources.

11. Visit ***alphafold.ebi.ac.uk***.
12. Paste the UniProt Entry number from above into the search bar.
13. Observe the predicted 3D structure.
14. Use the color coding to evaluate confidence in different parts of the structure.
15. Grab the axis tool in the lower left corner to rotate the model and see the complete structure.

## Reflection

1. Describe the protein structure (any patterns like coils, sheets, or helices).
   *Example answer: "The structure has a lot of coiled shapes that look like spirals. Those are alpha helices. I also saw some flat, arrow-like shapes called beta sheets. The protein looks folded up like a tangle of ribbons."*

2. What parts of the protein are predicted with high confidence? Which are not?
   *Example answer: "The middle part of the protein is dark blue, which means AlphaFold is very confident in that part of the structure. The ends of the protein are yellow or orange, which means less confidence there."*

3. Why do you think some parts of the protein might be harder to predict?
   *Example answer: "Some parts of the protein move around more or don't have a fixed shape, so they're harder for Alphafold to predict. Also, if there is not a lot of data from similar proteins, the model might not know what shape to expect."*

4. How might the shape of the protein help it carry out its function in the immune system?

   *Example answer: "The shape is important because it lets the protein bind to other molecules, like parts of bacteria or viruses. For example, receptors like TLRs have a specific shape that helps them recognizes patterns on the invaders (cell wall)."*

5. Compare your protein structure with another student. How are their structures and lengths different? Why might that be?

   *Example answer: "Antibody and TLR. The antibody was shorter and had a Y-shape that helps it stick to antigens. The TLR was much longer and had a curved shape that probably helps it sit on the surface of a cell and recognize invaders. Different proteins have different jobs, so their shapes and sizes are different."*