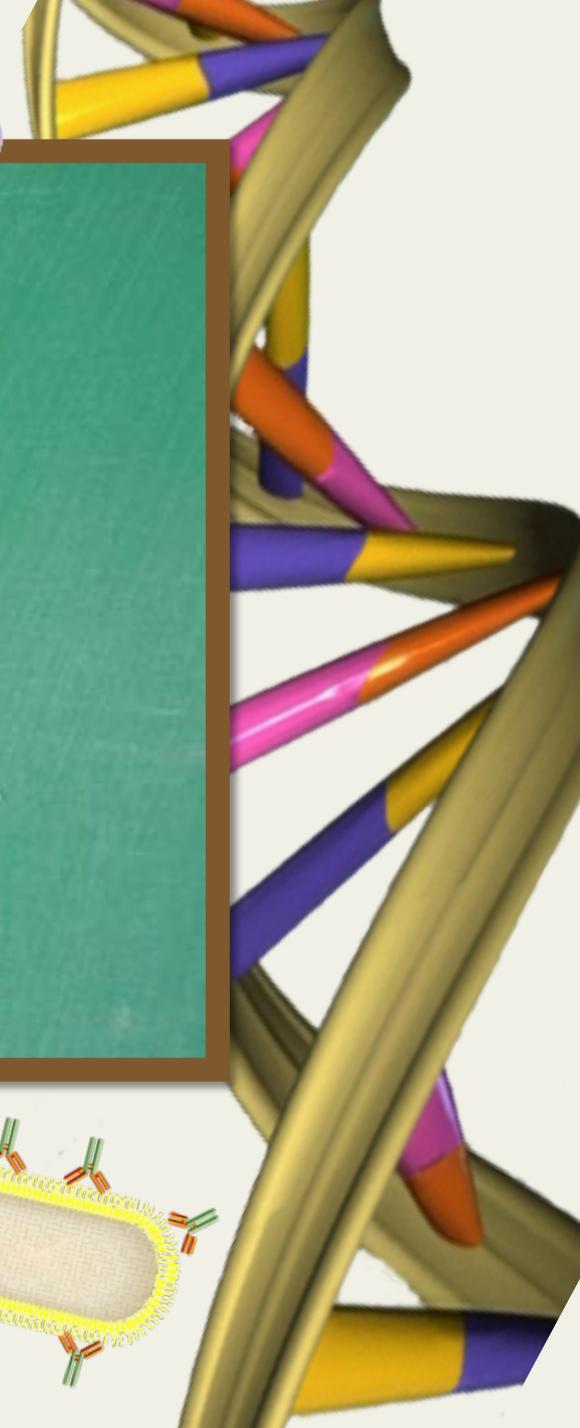
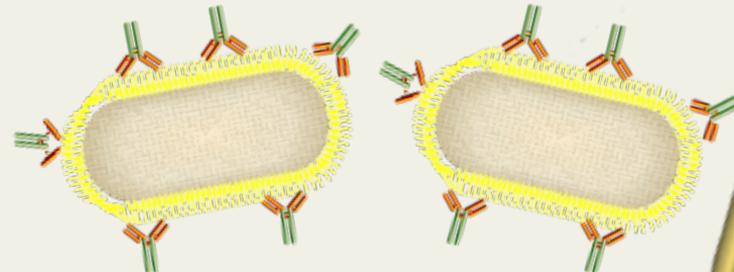




Immunity & Disease



What is DNA?



What is DNA Day?

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April 1953

Drs. James Watson and
Francis Crick determined
the **structure of DNA**
(double helix)

What is DNA Day?



April 1953

Drs. James Watson and Francis Crick determined the **structure of DNA** (*double helix*)



April 2003

Human Genome Project determined the **entire DNA sequence of a human** (*3 billion letters*)

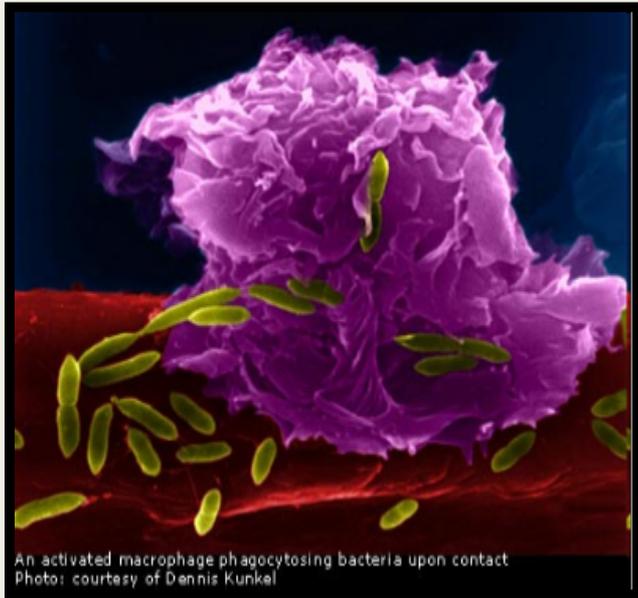
What is the Immune System?

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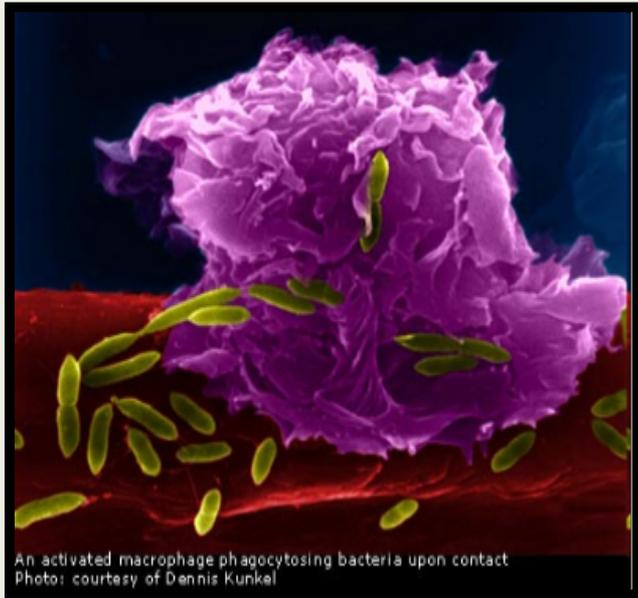


A macrophage engulfing bacteria

What is a **pathogen**?

What is the Immune System?

The **immune system** protects the body from disease.



A macrophage engulfing bacteria

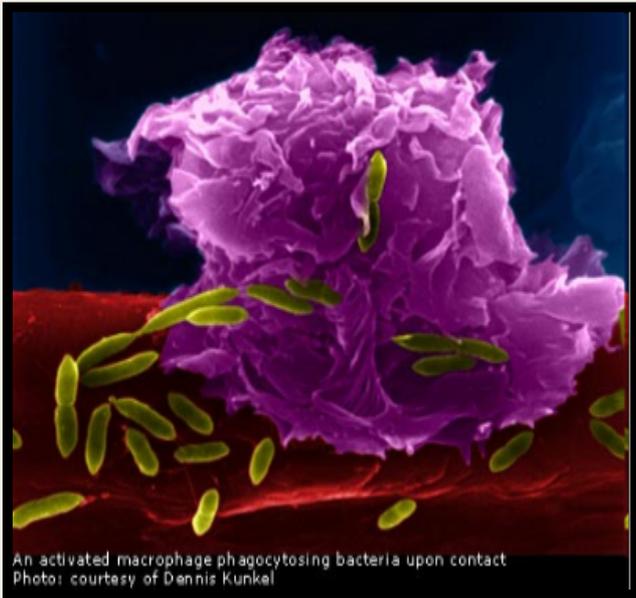
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An infectious organism that can cause disease.

Examples: bacteria, viruses, fungi, and parasites

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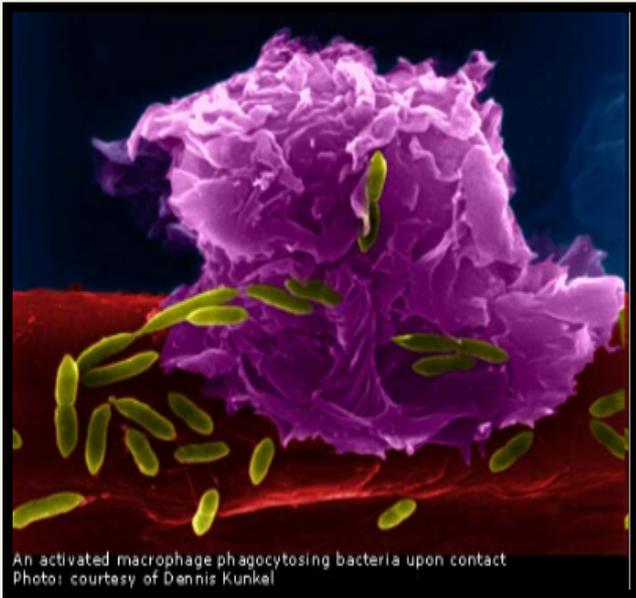
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What is a **pathogen**?

An infectious organism that can cause disease.

Examples: bacteria, viruses, fungi, and parasites

Are humans the only ones with an immune system?

No, other mammals, plants, fish, reptiles, and insects all have immune systems.

What happens when we get an infection?

*Our immune system destroys the pathogen in **2 ways***

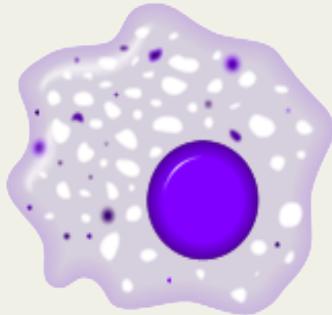
What happens when we get an infection?

*Our immune system destroys the pathogen in **2 ways***

1. Cell-mediated response – involves our immune cells to destroy pathogens

Examples:

Macrophage



Eat pathogens and debris

Neutrophils

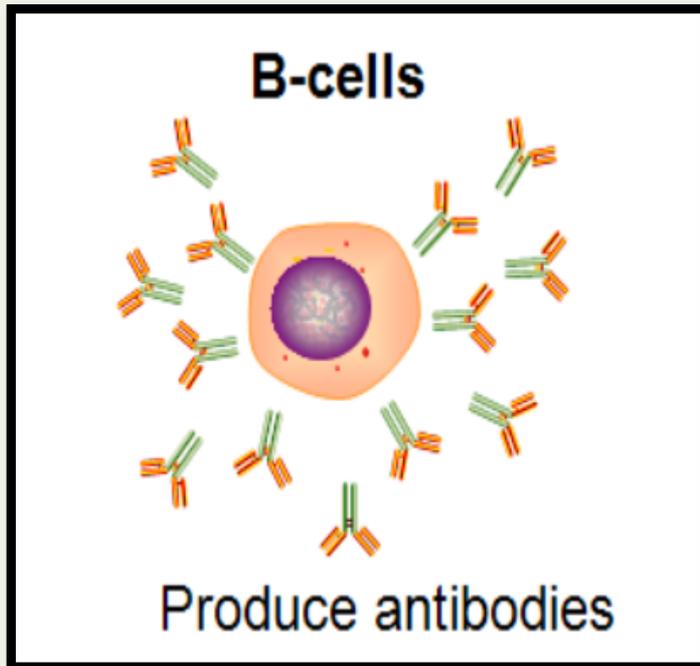


Eat pathogens and kill by releasing toxic particles

What happens when we get an infection?

*Our immune system destroys the pathogen in **2 ways***

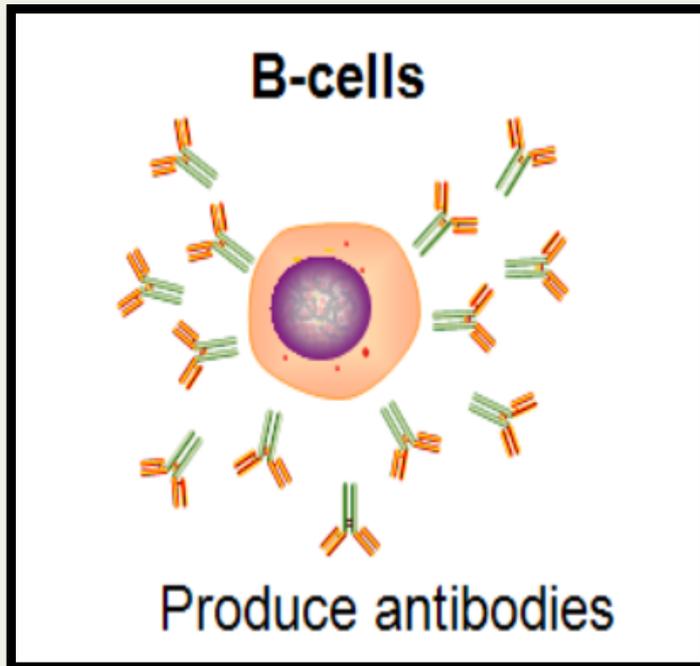
2. Humoral response – destroy pathogens using antibodies produced by B cells



What happens when we get an infection?

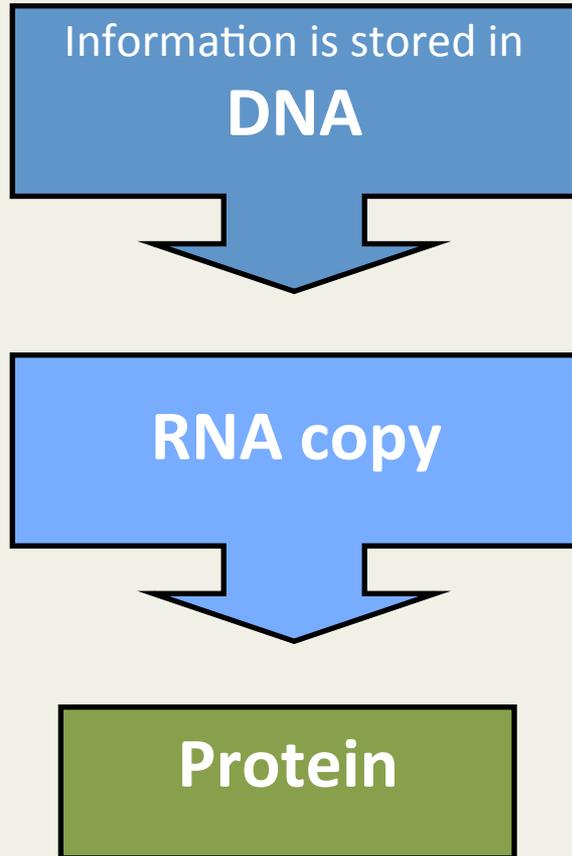
*Our immune system destroys the pathogen in **2 ways***

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What is an
antibody?

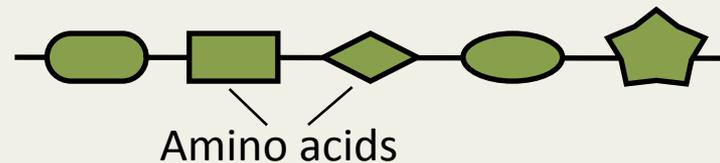
Antibodies are Proteins



RNA Synthesis
(transcription)

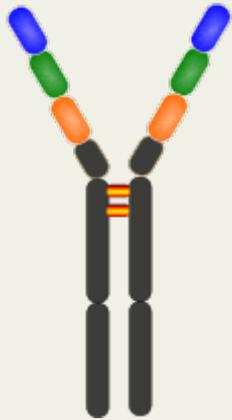


Protein Synthesis
(translation)

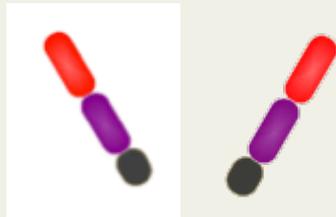


Proteins do most of the work in a cell and provide much of its structure

Antibody Structure

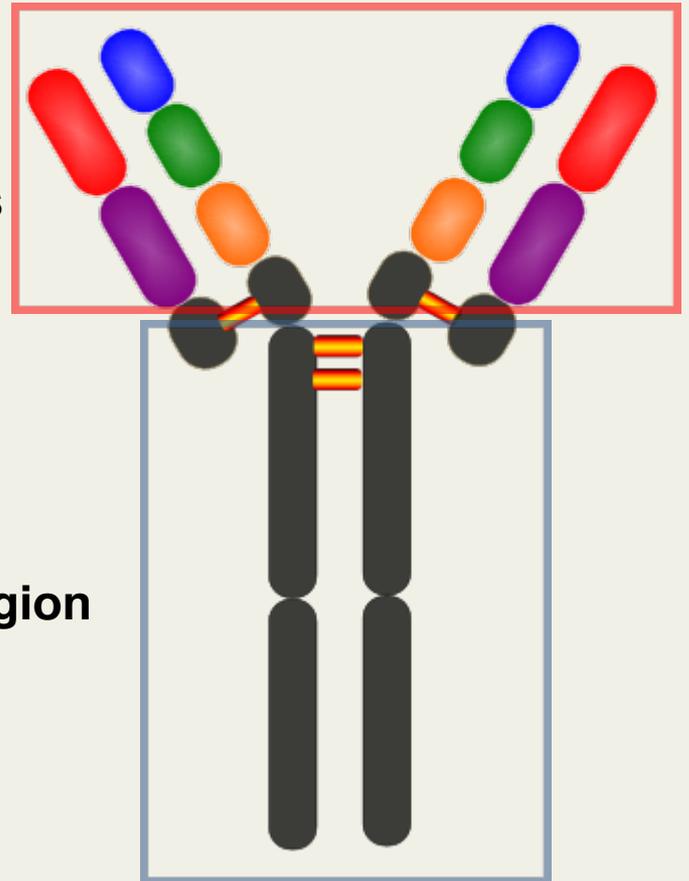


Heavy Chain



Light Chain

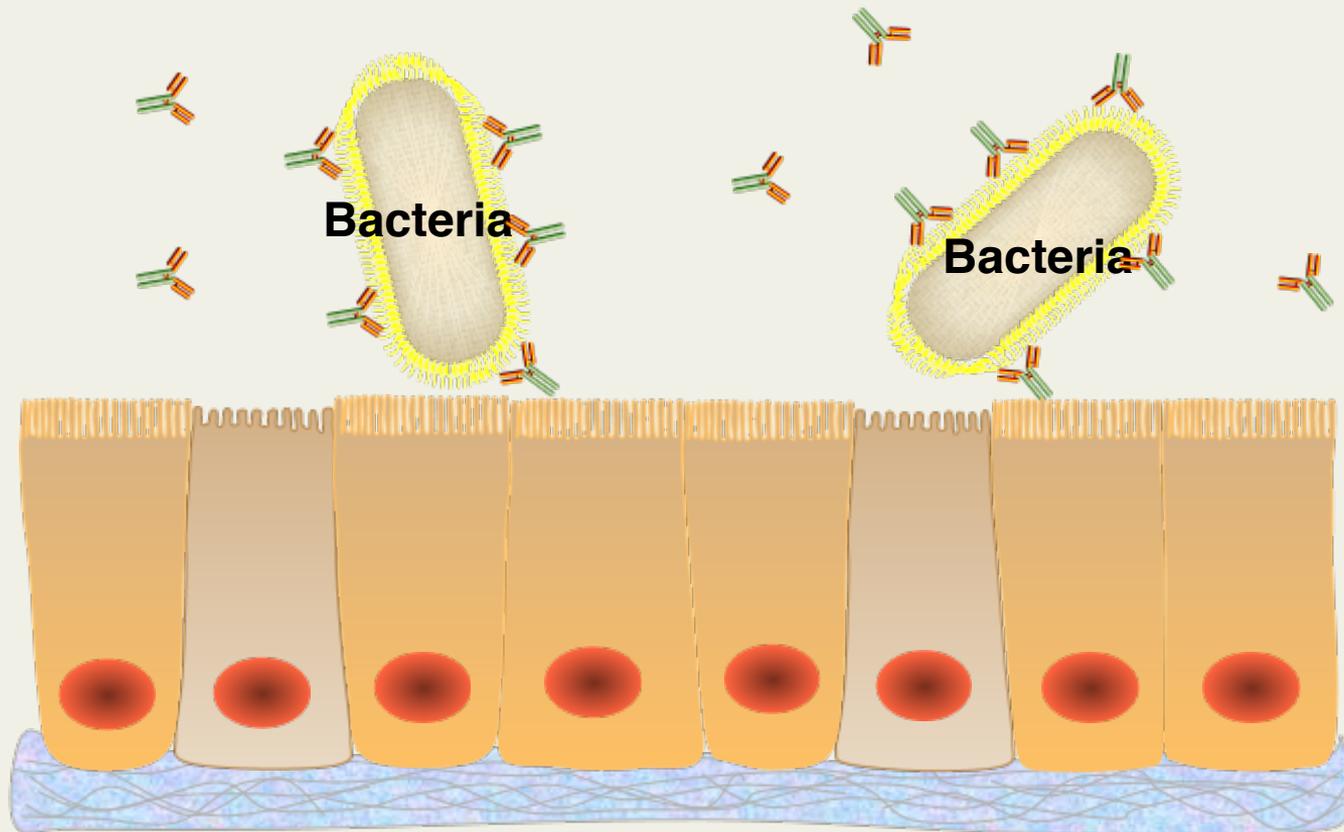
Variable Region:
Part of the antibody
that binds Pathogens



Constant Region

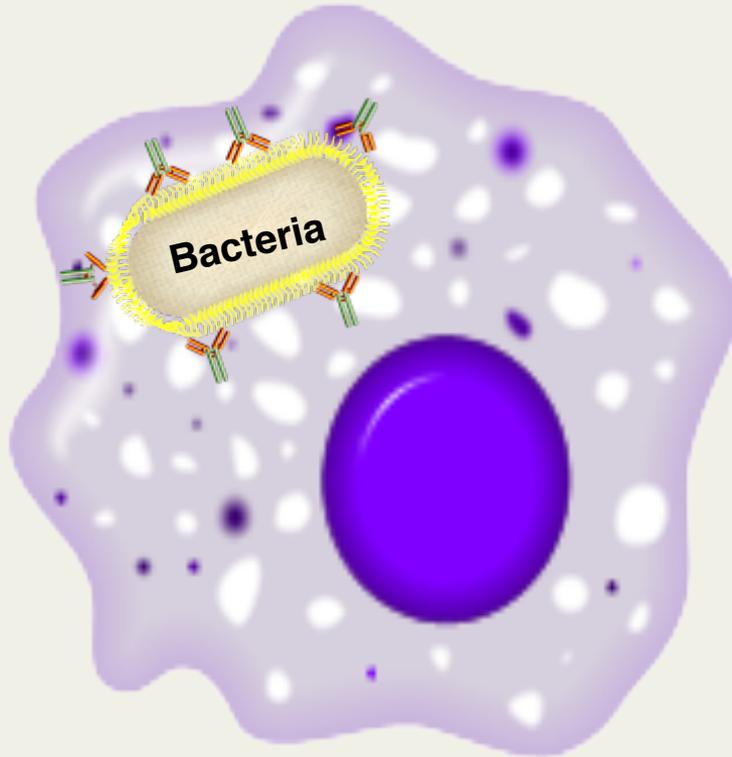
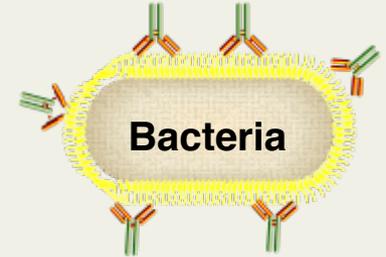
What do Antibodies do?

1. Prevent pathogens from binding cells

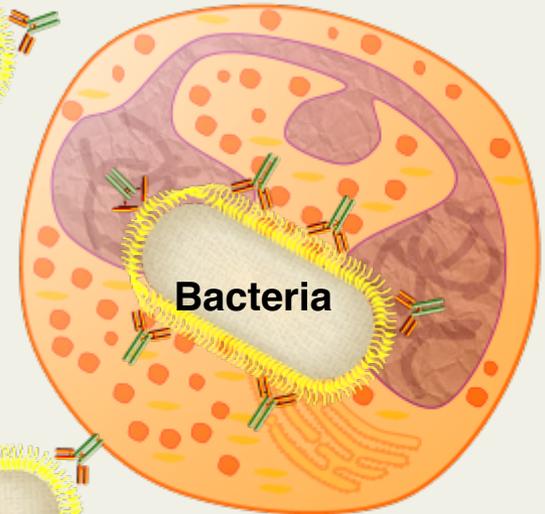
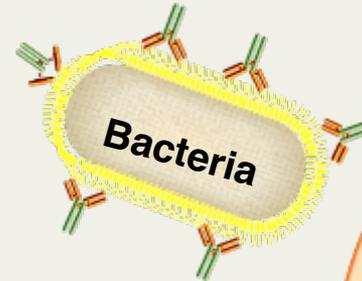


What do Antibodies do?

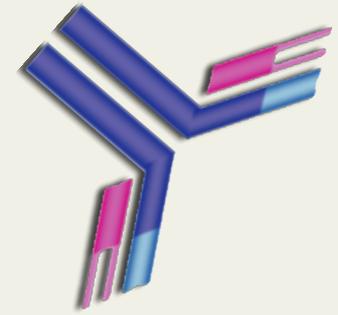
2. Help other cells recognize pathogens so they can eat them up



Macrophage

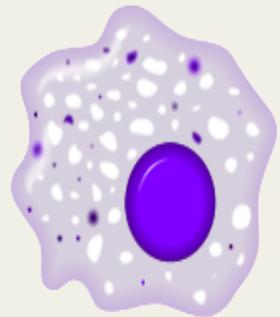


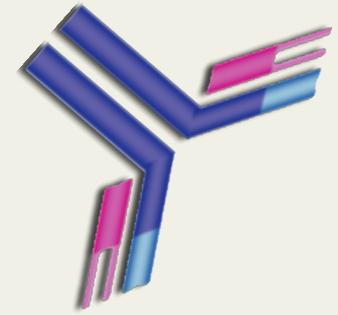
Neutrophil



Questions...

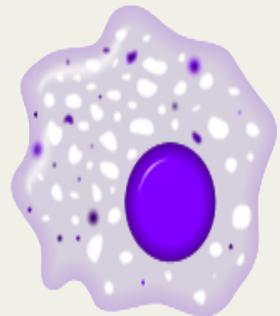
1. Name some pathogens that can infect us and cause disease?

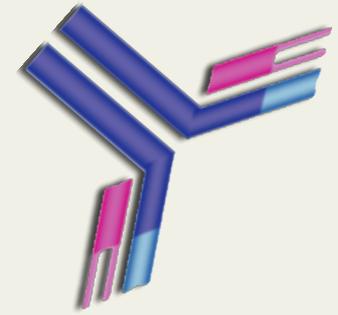




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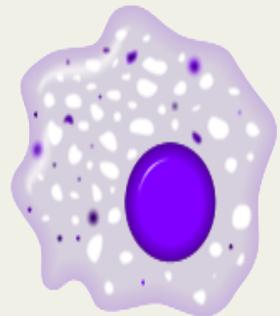
1. Name some pathogens that can infect us and cause disease?
2. If there are several types of pathogens, do they all look similar or different?





Questions...

1. Name some pathogens that can infect us and cause disease?
2. If there are several types of pathogens, do they all look similar or different?
3. If there are several pathogens different from each other, how do our antibodies recognize and bind all of them?



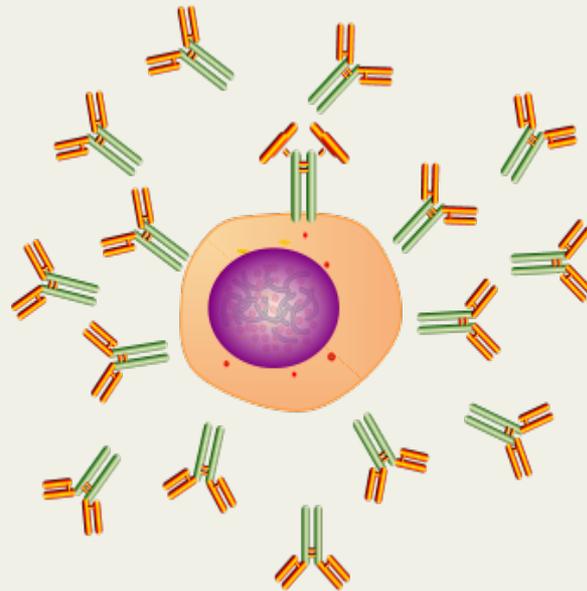
Immunity Demonstration

**There are LOTS of different
pathogens.**

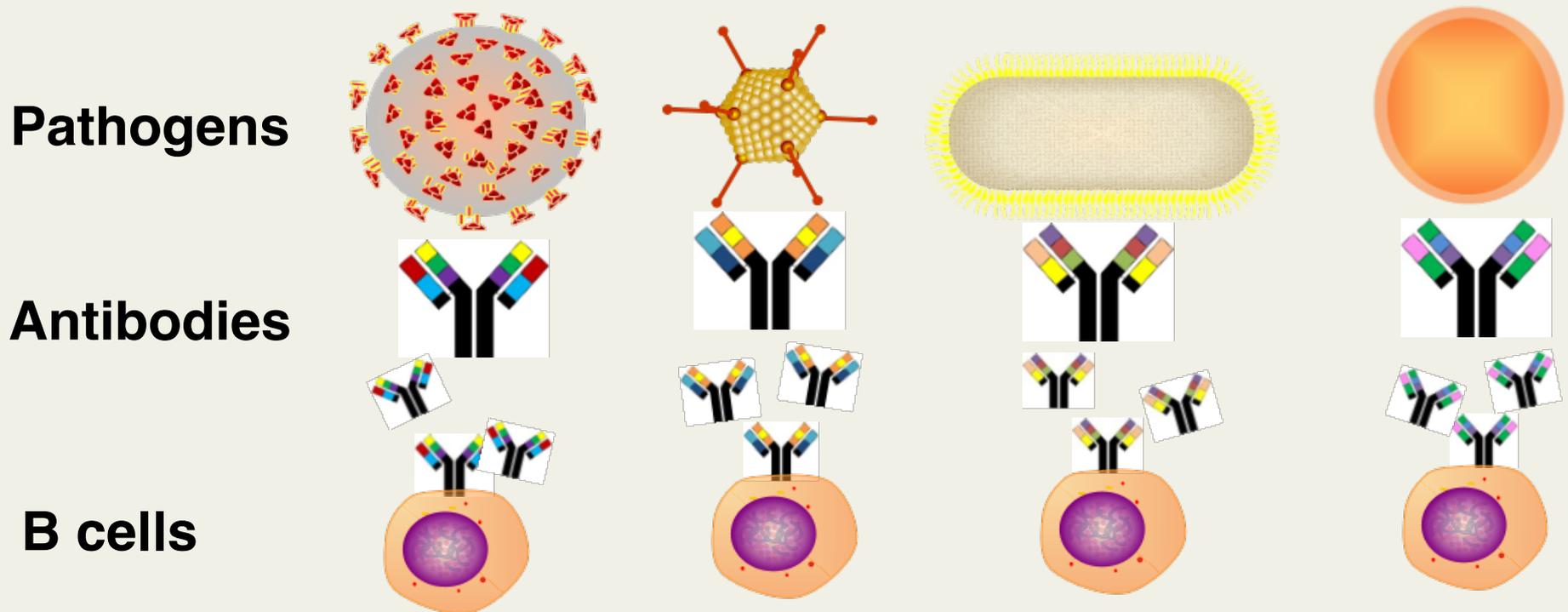
**How does our immune system
recognize them all?**

Remember....

B cells are the cells of the immune system
that make antibodies

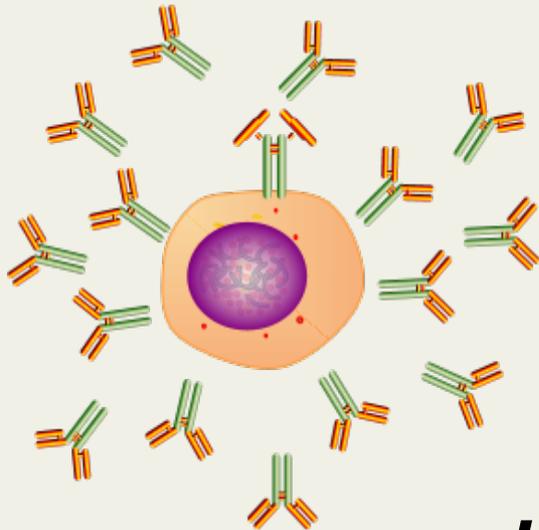


Each B cell produces a **unique** antibody that recognizes a **specific** piece of foreign material (e.g., pathogen)



The different antibodies are unique from each other by having **different variable regions!**

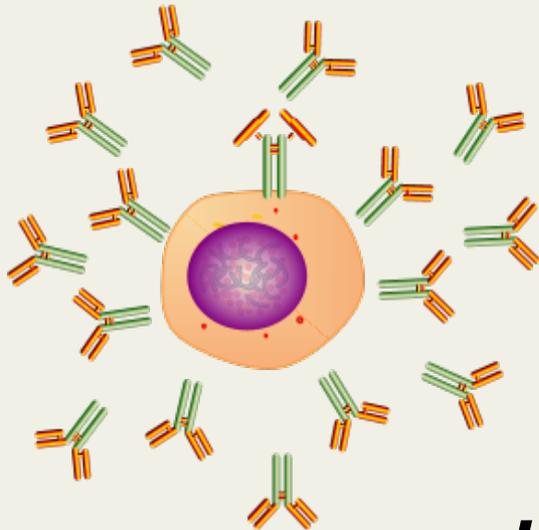
How do B cells produce different variable regions of antibodies?



Our B cells can make 10^{11} different antibodies.

How many is this?

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Our B cells can make 10^{11} different antibodies.

How many is this?

100,000,000,000

Could it be that in our DNA we have a **gene** for each of these 10^{11} **antibodies**?



The entire human genome contains about 30,000 genes

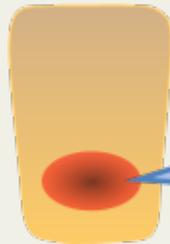
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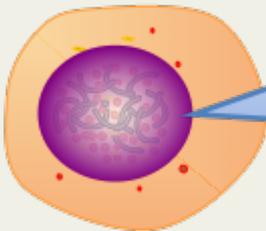
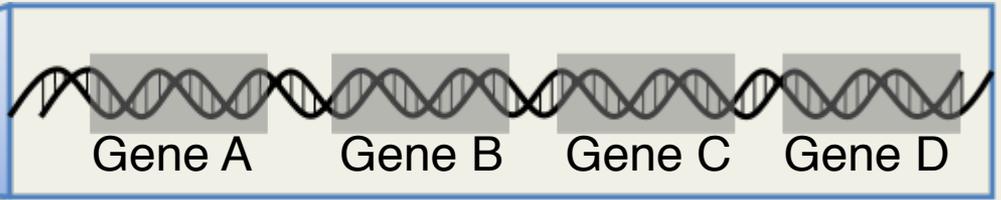
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30,000 \lll 100,000,000,000
(30,000 is much less than 100,000,000,000)

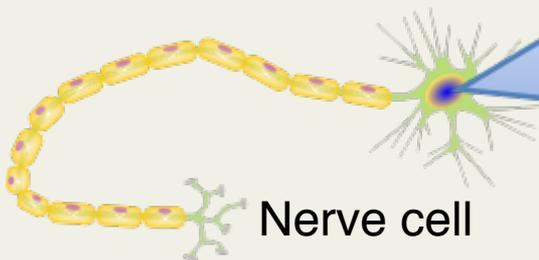
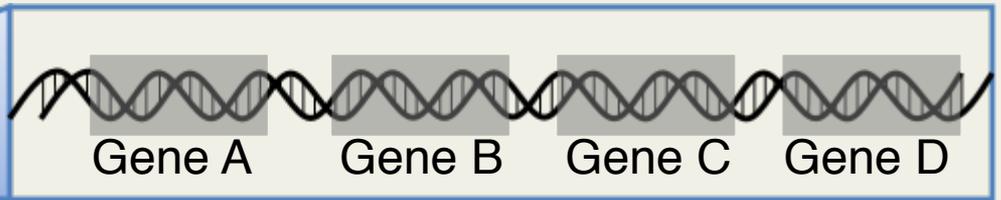
Every cell in your body has the exact same genetic information encoded in your DNA



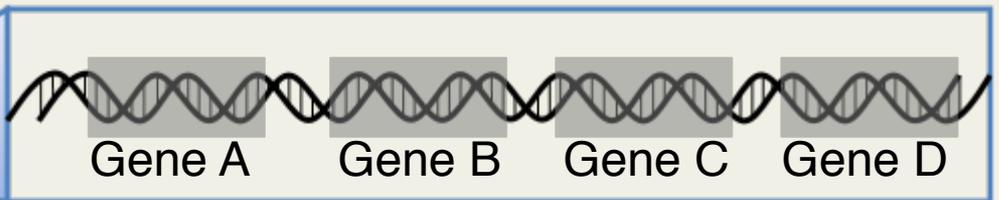
Skin cell



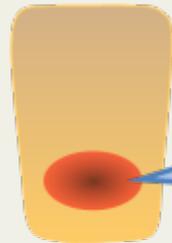
B cell



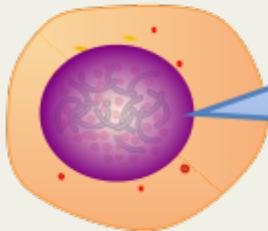
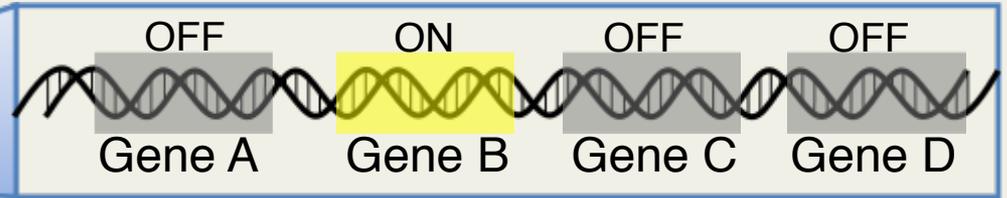
Nerve cell



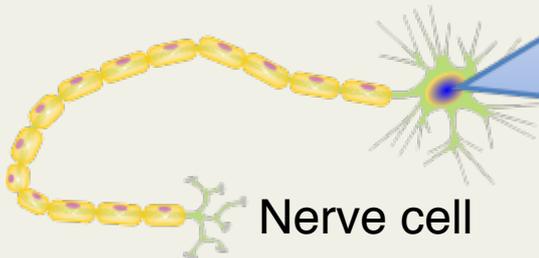
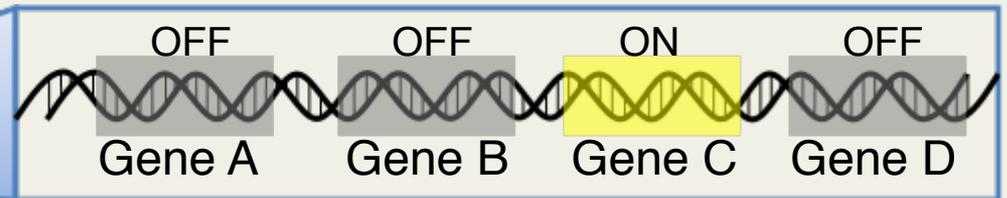
However, different cells have different genes turned on or off



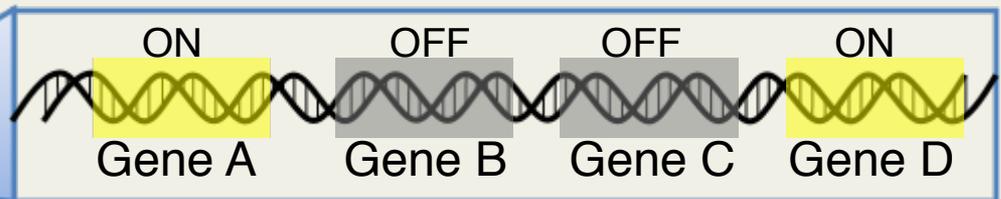
Skin cell



B cell



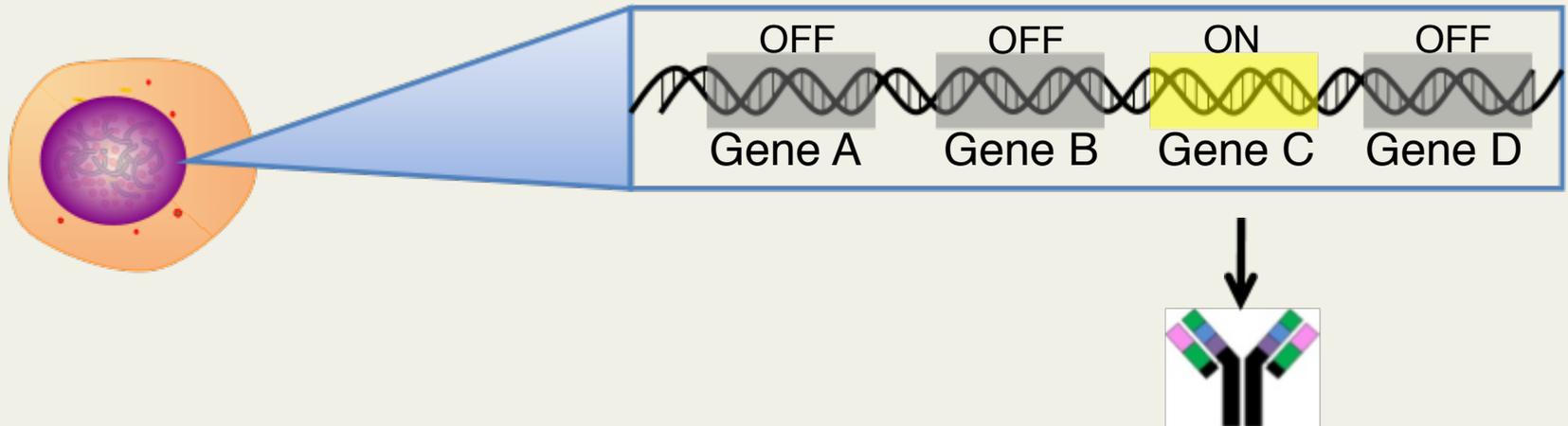
Nerve cell



How do B cells produce different variable regions of antibodies?

Part of the answer is that....

In the DNA of B cells, specific antibody genes are turned on.



How do B cells produce different variable regions of antibodies?

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- We are able to make so many different antibodies due to another phenomenon called **VDJ Recombination**

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- **VDJ recombination** is the process by which V, D, and J genes are randomly selected and combined to form the heavy and light chains that make antibodies.

How do B cells produce different variable regions of antibodies?

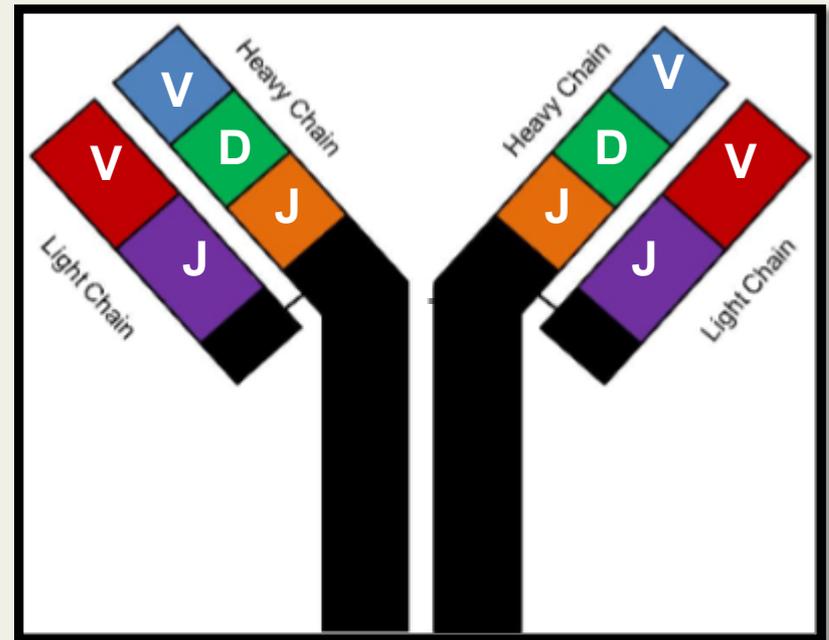
- We are able to make so many different antibodies due to another phenomenon called **VDJ Recombination**
- **VDJ recombination** is the process by which V, D, and J genes are randomly selected and combined to form the heavy and light chains that make antibodies.
- **VDJ recombination** is specific to certain cells of the immune system and does not occur in other cells of our body.

Genes that encode antibody proteins are found in DNA

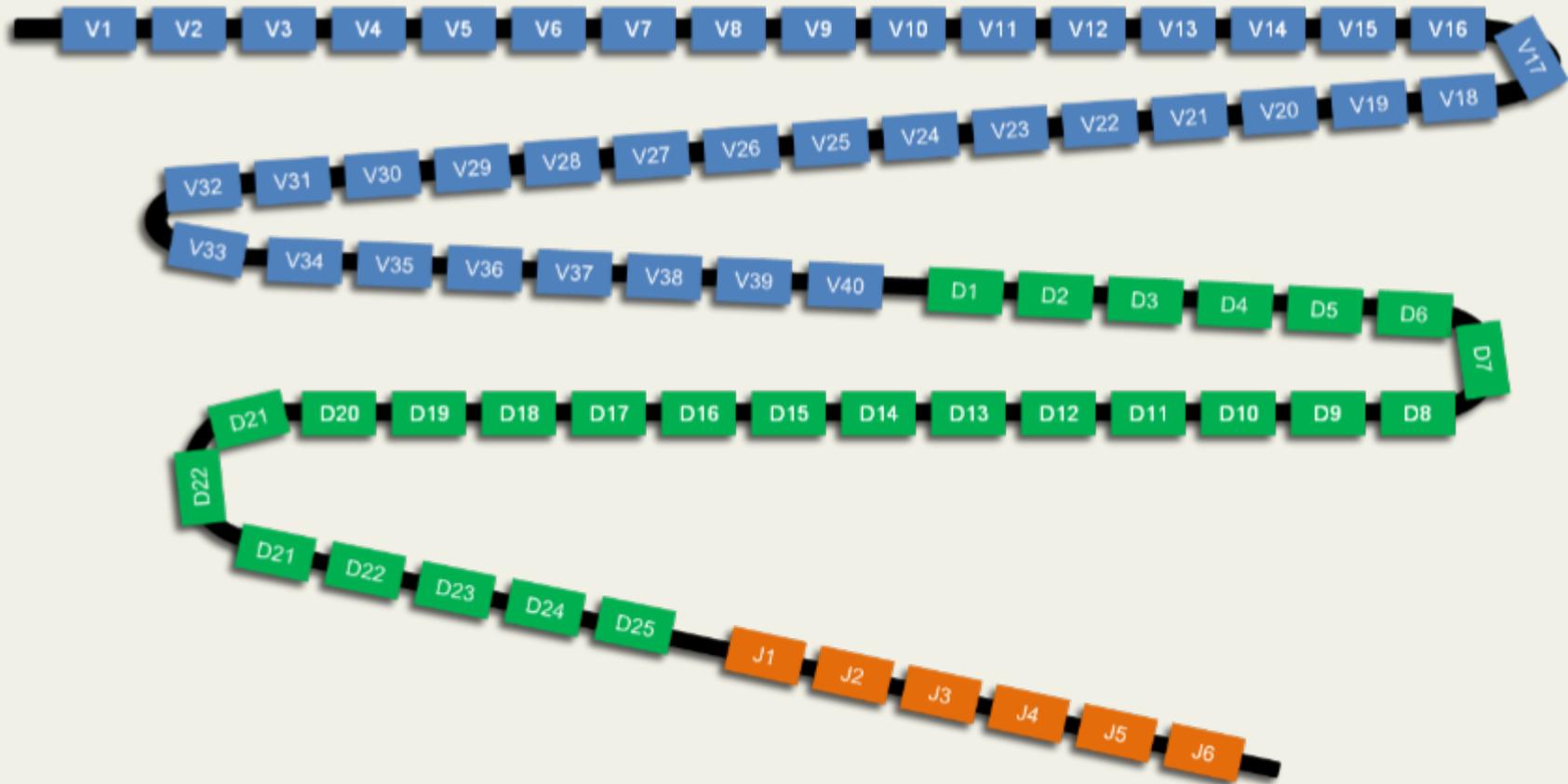
- Antibodies are made up of 2 light chain proteins and 2 heavy chain proteins.

Genes that encode antibody proteins are found in DNA

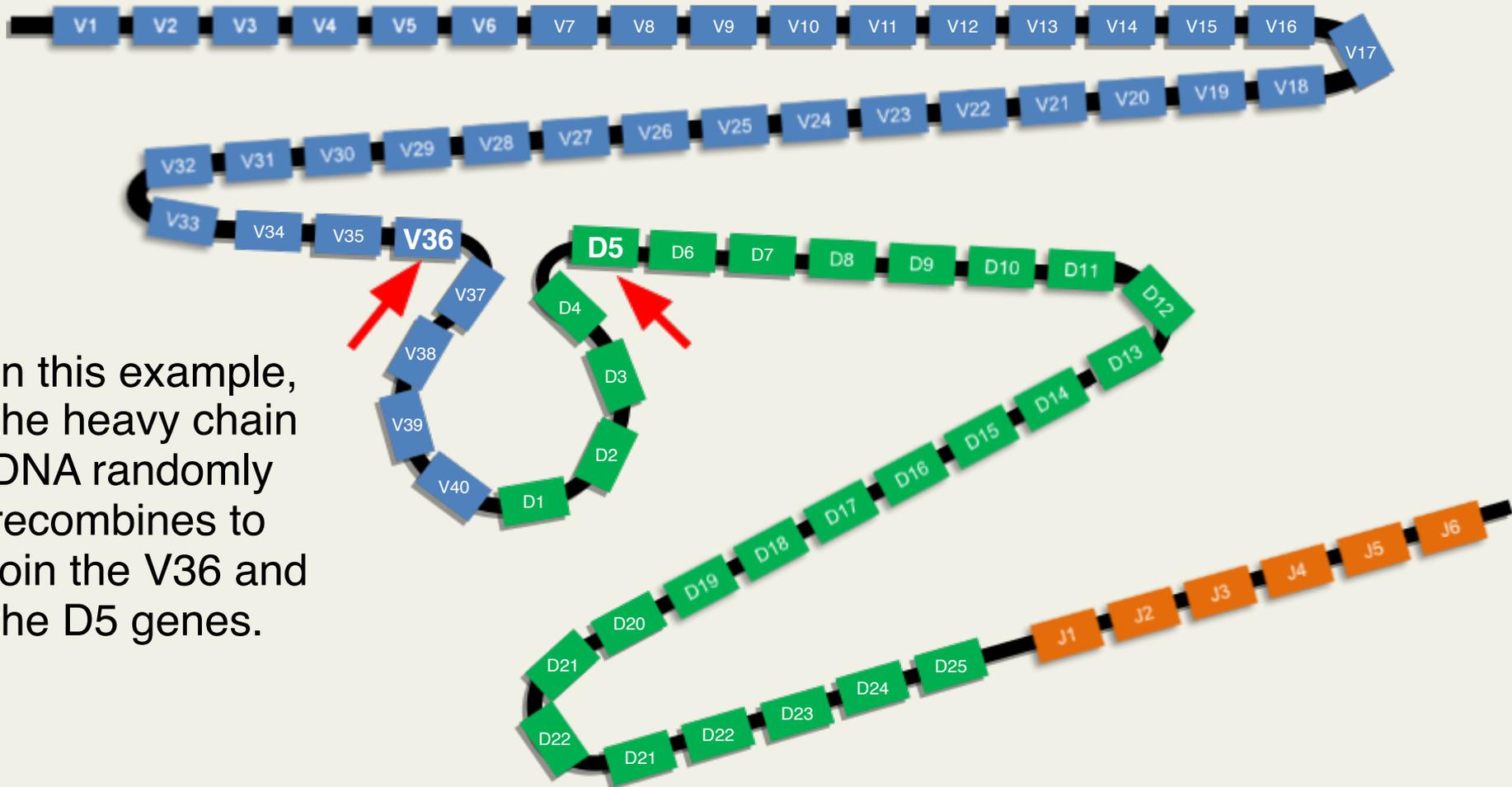
- Antibodies are made up of 2 light chain proteins and 2 heavy chain proteins.
- The genes that encode these proteins are found in your DNA. These are referred to as **V**, **D**, and **J** genes.



There are 45 V, 27 D, and 6 J genes in the heavy chain DNA sequence

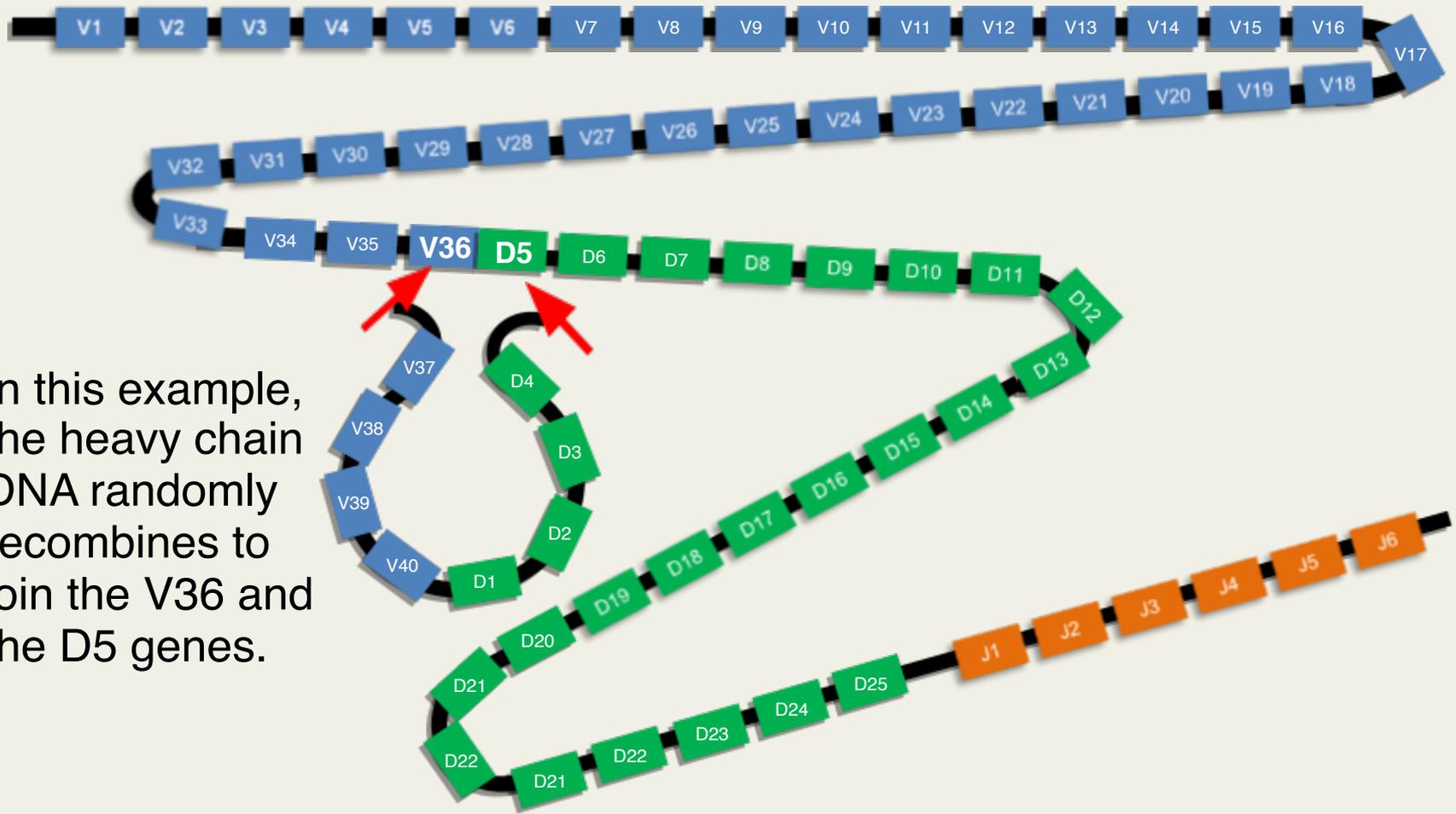


Through VDJ recombination, the cell randomly chooses 1 V, 1 D, and 1 J gene to make the heavy chain



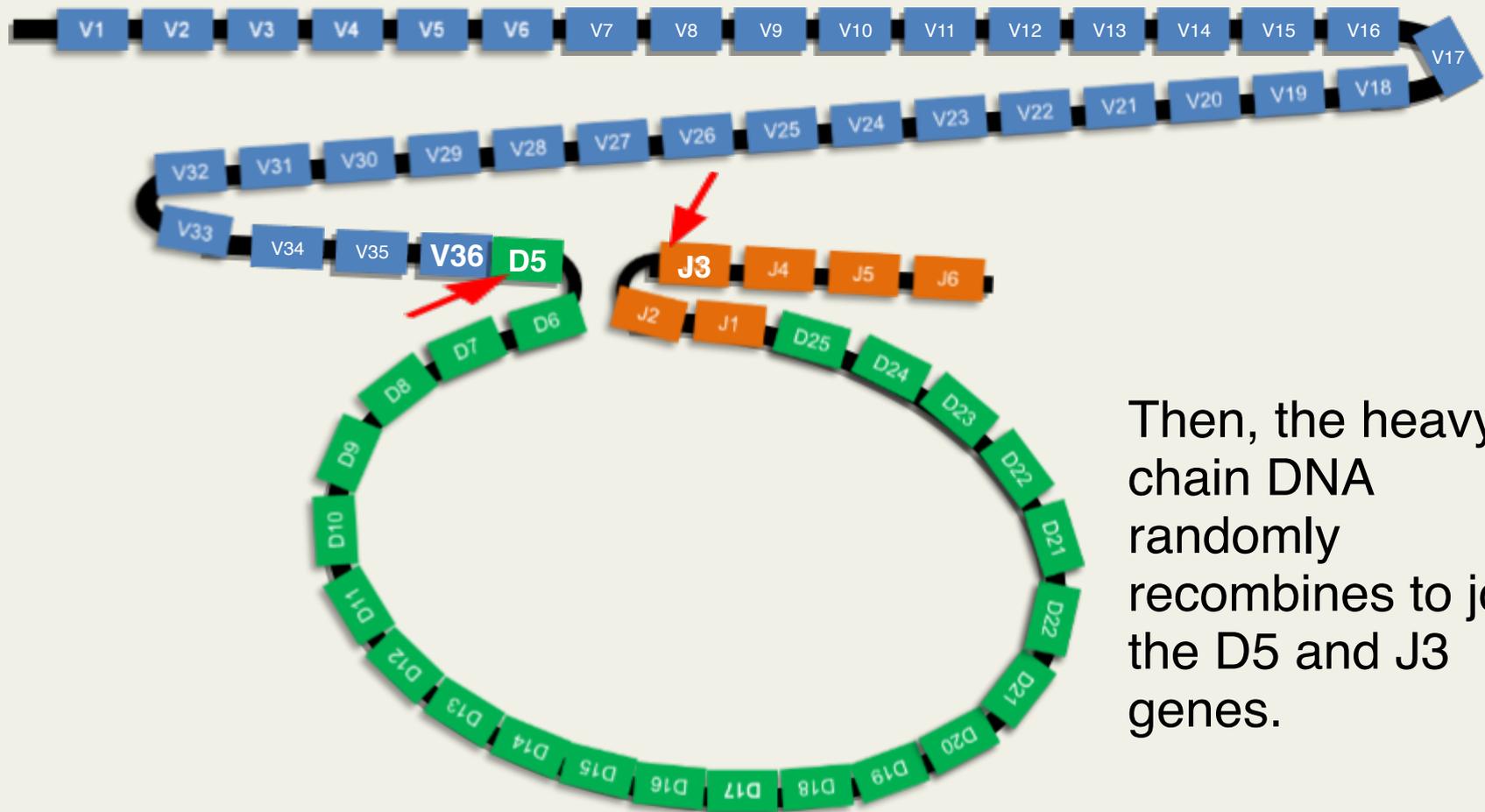
In this example, the heavy chain DNA randomly recombines to join the V36 and the D5 genes.

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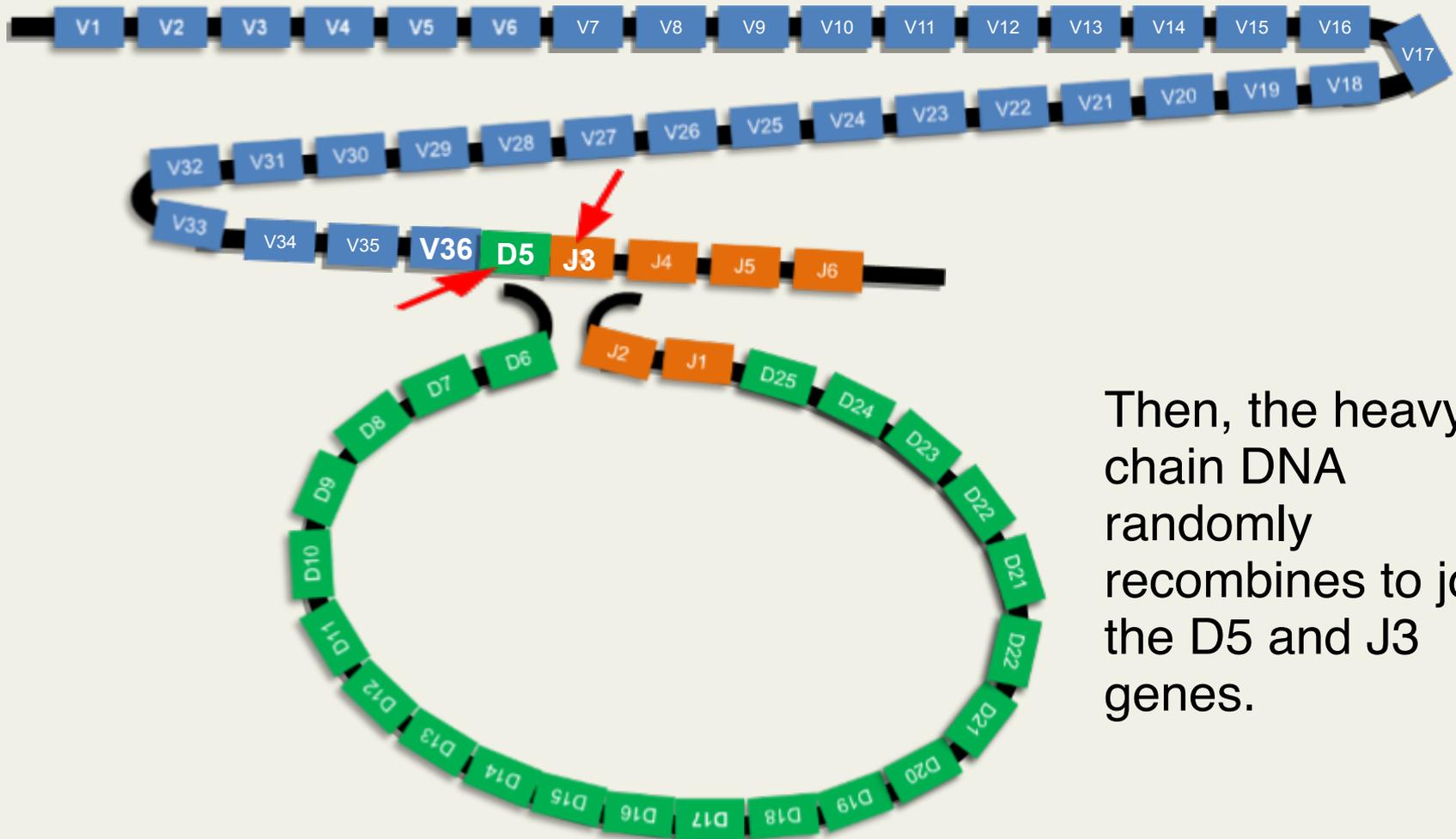
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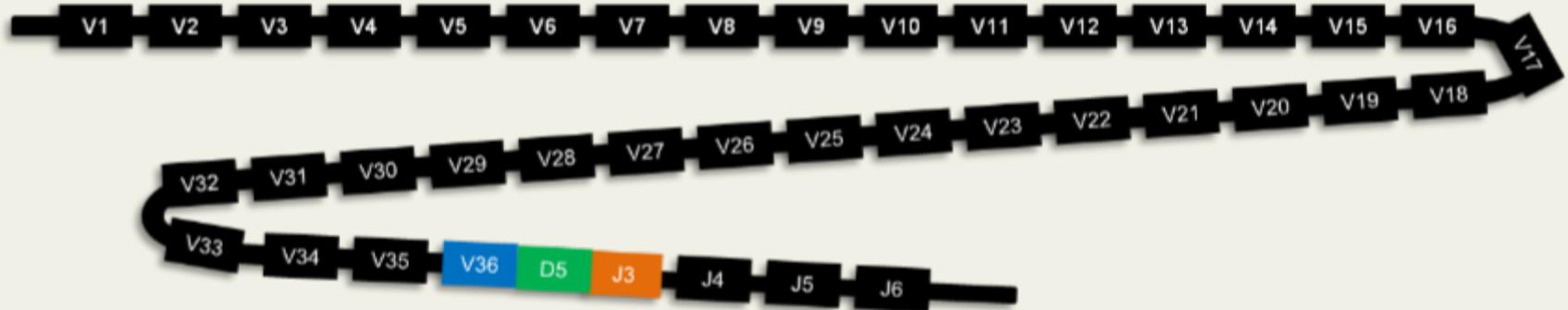
Then, the heavy chain DNA randomly recombines to join the D5 and J3 genes.

The cell randomly chooses 1 V, 1 D, and 1 J gene to make the heavy chain



Then, the heavy chain DNA randomly recombines to join the D5 and J3 genes.

DNA → RNA → Protein



Heavy chain DNA



Heavy chain mRNA

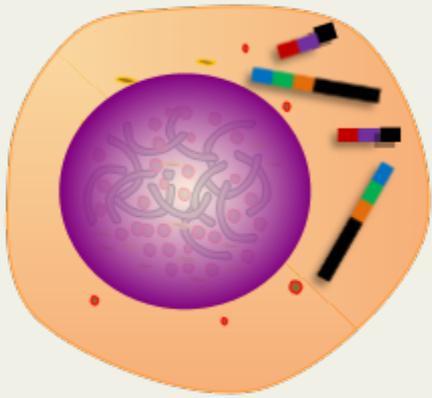


Heavy chain protein

Only the V36, D5 and J3 genes are turned **ON**.

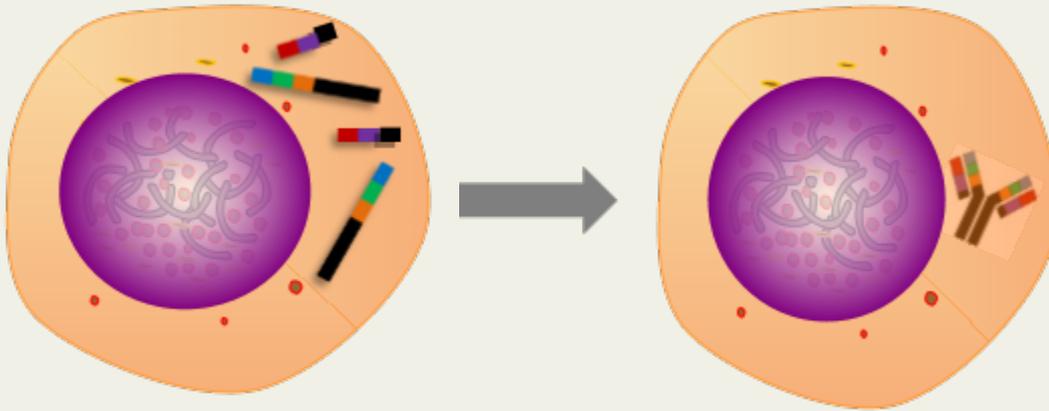
The remaining heavy chain genes are turned **OFF**.

Antibodies made and assembled in B-cells



Heavy and light chain
proteins are translated

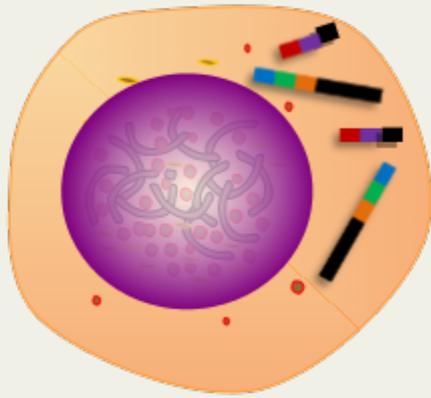
Antibodies made and assembled in B-cells



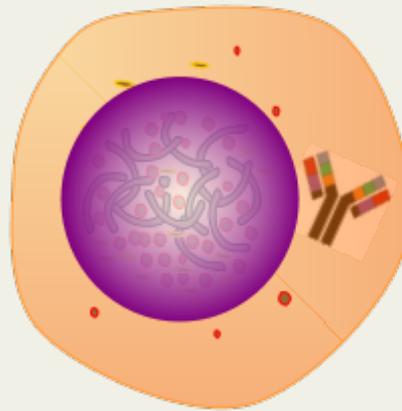
Heavy and light chain proteins are translated

Heavy and light chain proteins are assembled into antibodies within the cytoplasm

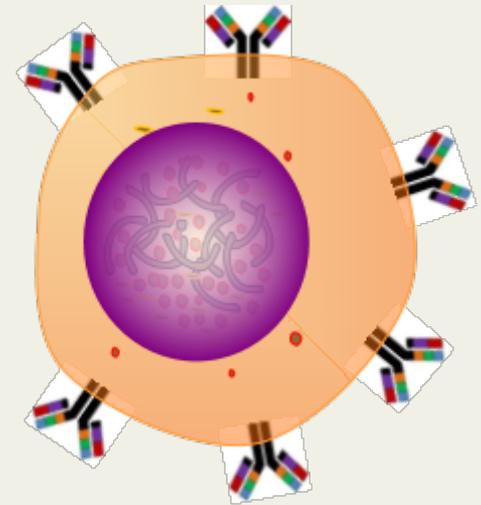
Antibodies made and assembled in B-cells



Heavy and light chain proteins are translated

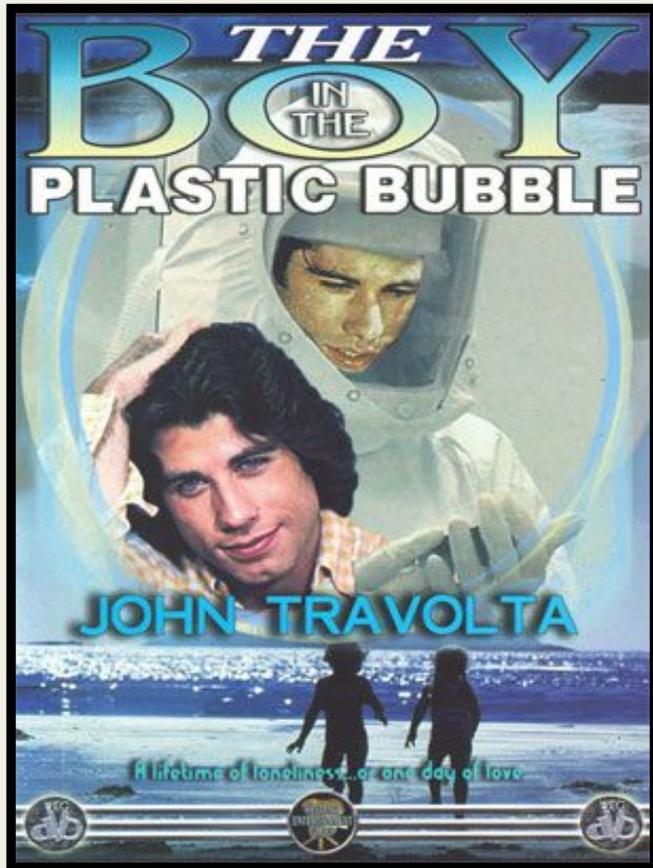


Heavy and light chain proteins are assembled into antibodies within the cytoplasm



Antibodies are exported to the cell surface where they can recognize pathogens

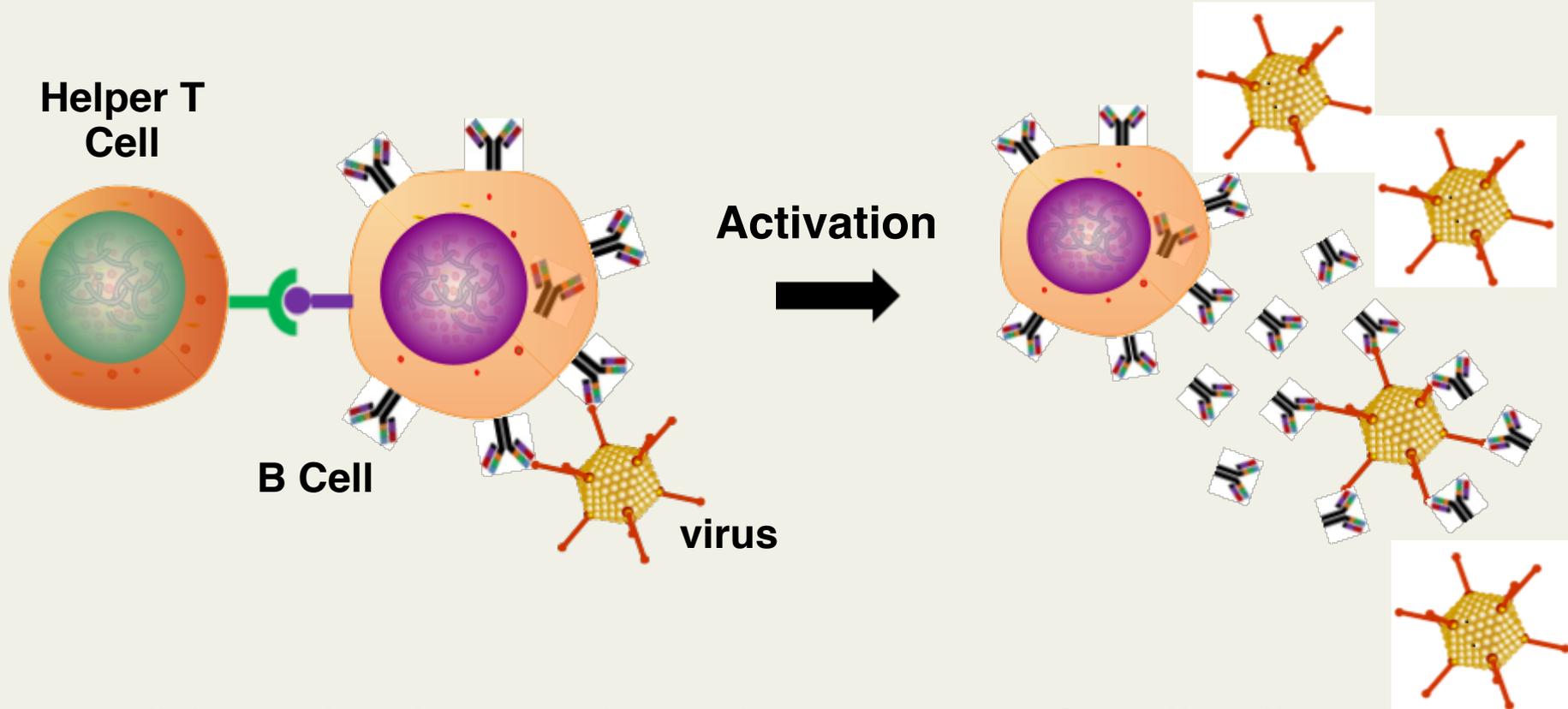
The inability of immune cells to perform VDJ recombination has very serious consequences!



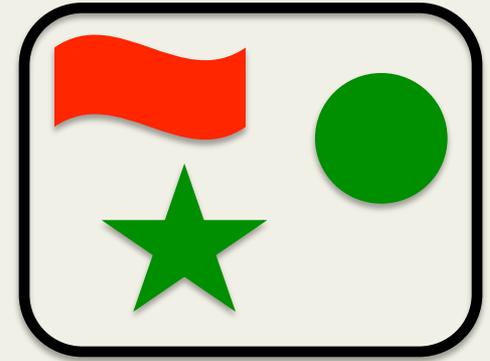
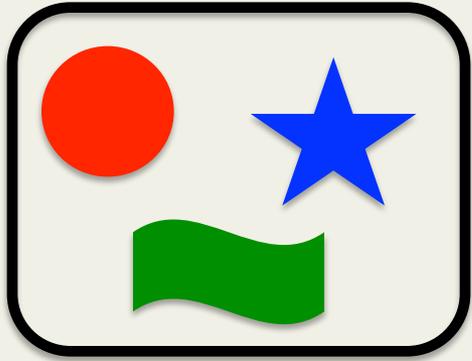
Individuals with a defect in VDJ recombination, lack diversity in their antibody production, and as a result have severely weakened immune systems (**immunodeficiency**)

http://en.wikipedia.org/wiki/The_Boy_in_the_Plastic_Bubble

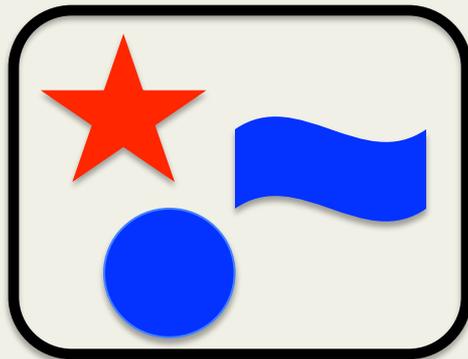
Once a B cell recognizes a pathogen, how does it trigger an immune response?



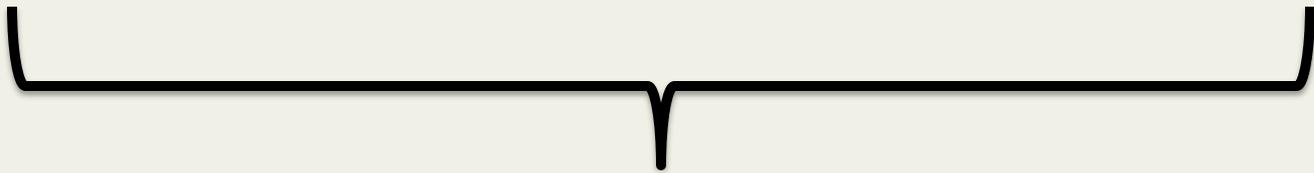
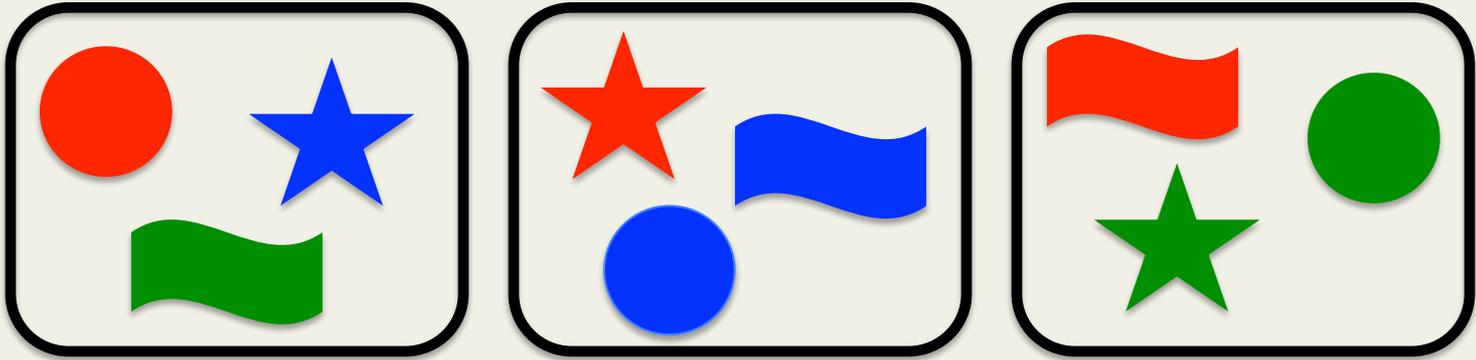
- This activation leads to the release of antibodies and **clonal expansion**.



VDJ Recombination Game



One student in each group will secretly create a unique pathogen

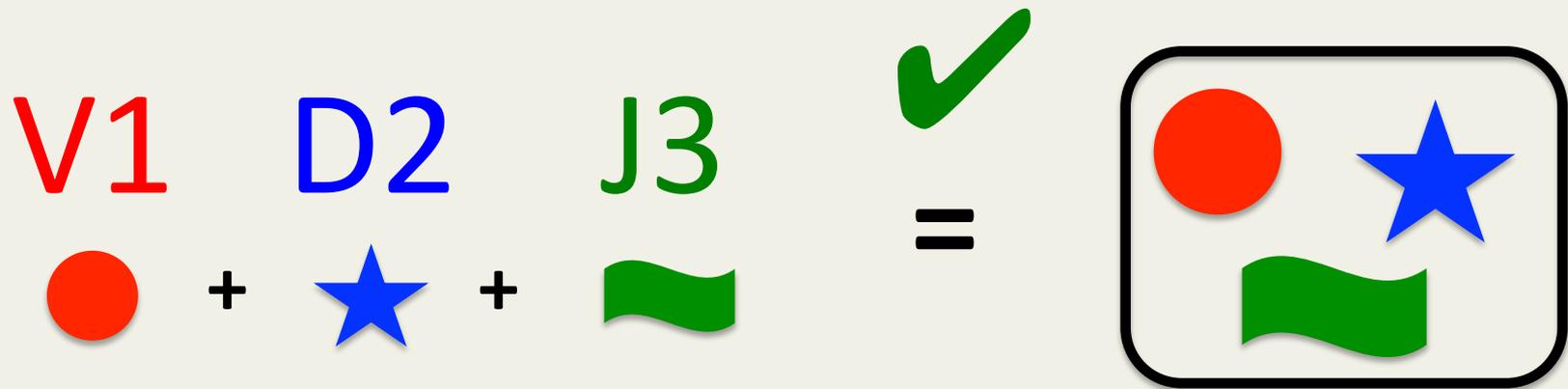


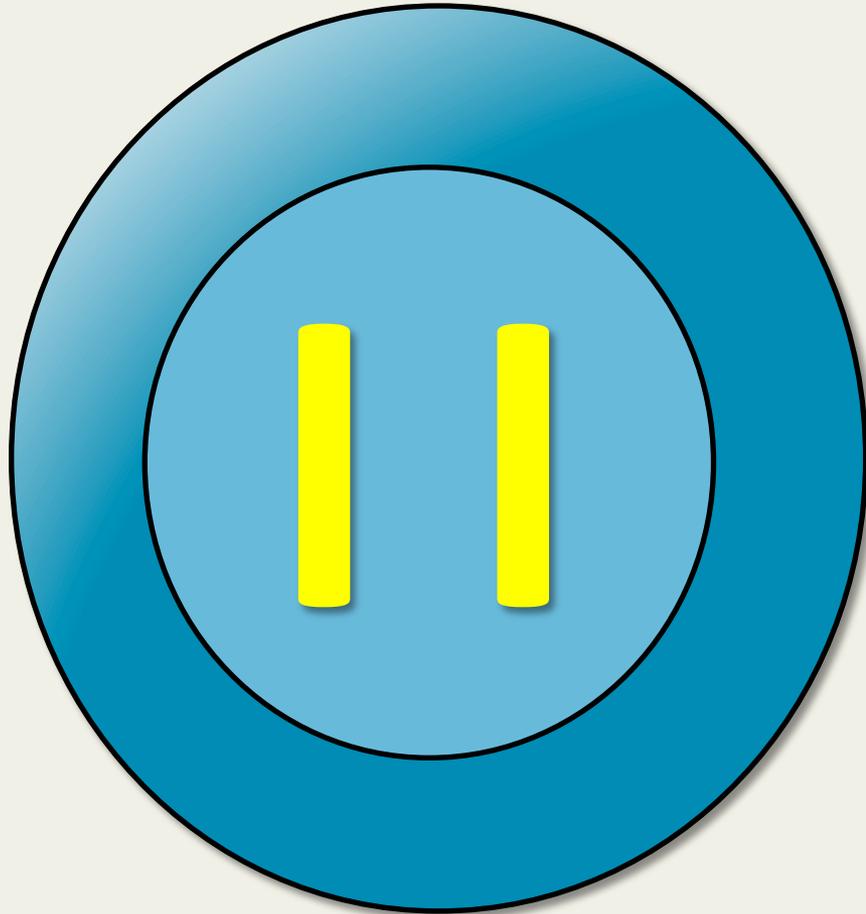
Example Pathogens!

One student in each group will choose one V, D and J gene to create a unique B-cell

V1 	V2 	V3 
D1 	D2 	D3 
J1 	J2 	J3 

The B-cell has FOUR chances to correctly match the pathogen!

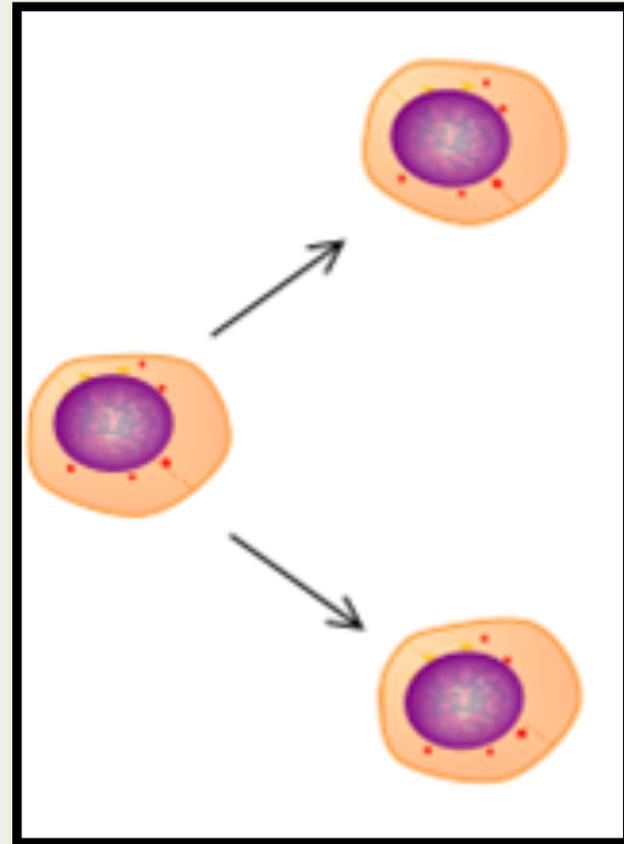




Please **PAUSE**
and take a
moment
to play the VDJ
recombination
game

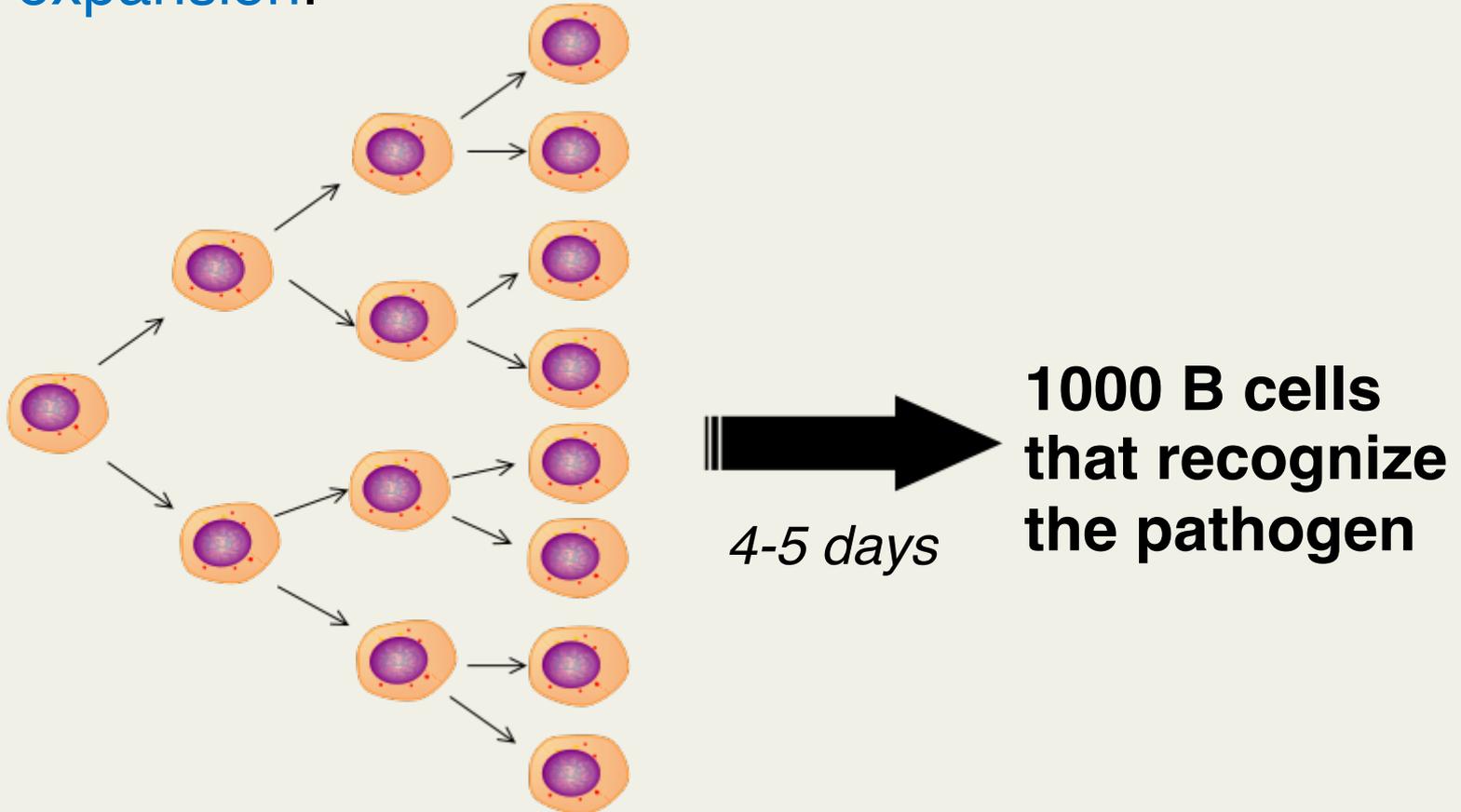
One B cell isn't going to release enough antibody on its own to fight a pathogen. So it makes clones of itself.

A **clone** is an exact genetic copy of another cell.



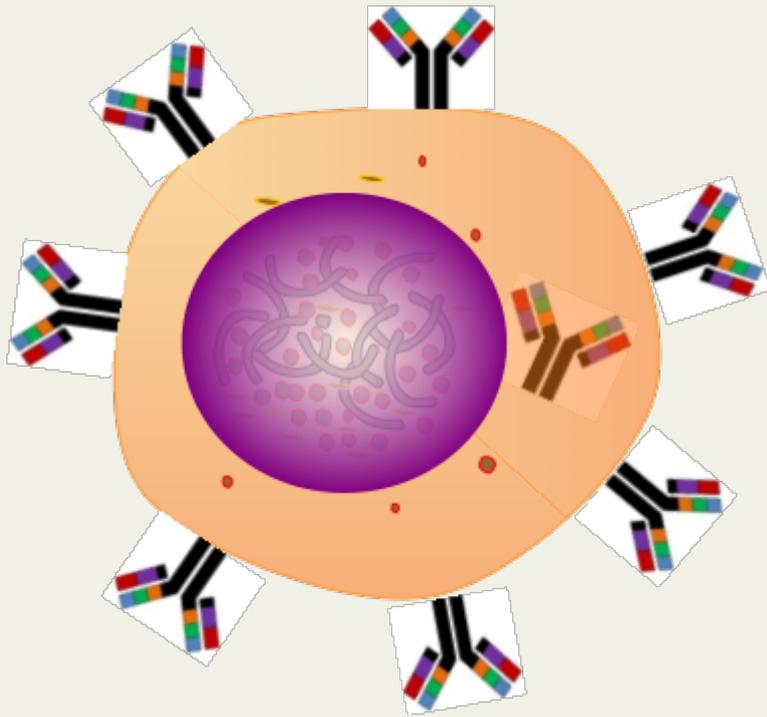
Clonal expansion

An activated B cell that has come in contact with its corresponding pathogen and helper T cell will go through **clonal expansion**.



Immunity Demonstration

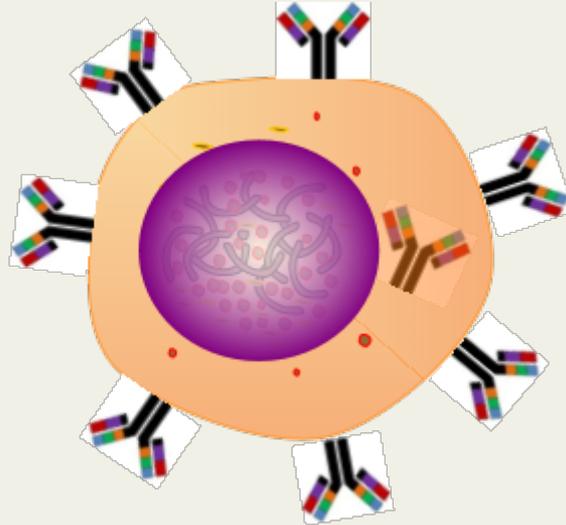
Memory B Cells



After clonal expansion, some B cells turn into **memory B cells**.

These cells will remain in your body for years, ready to respond immediately if you encounter that pathogen again.

Memory B Cells



Memory B cells protect us from future infections...

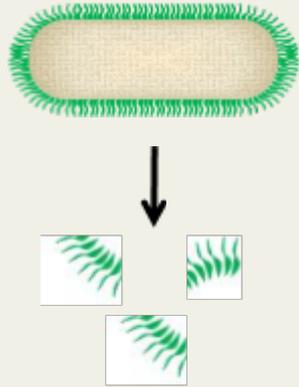
Can we take advantage of memory B cells to prevent ourselves from getting sick?

Vaccines help our bodies create **memory B cells** without making us sick

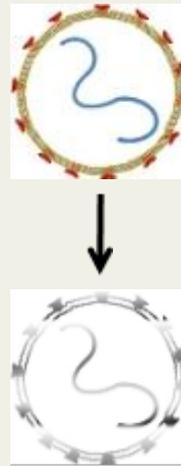


How do **vaccines** work?

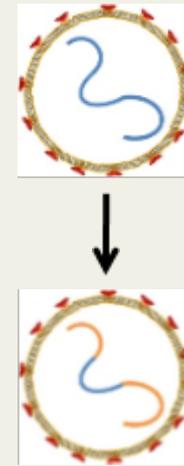
Vaccines contain non-infectious versions of a pathogen:



**Subunit
vaccines**



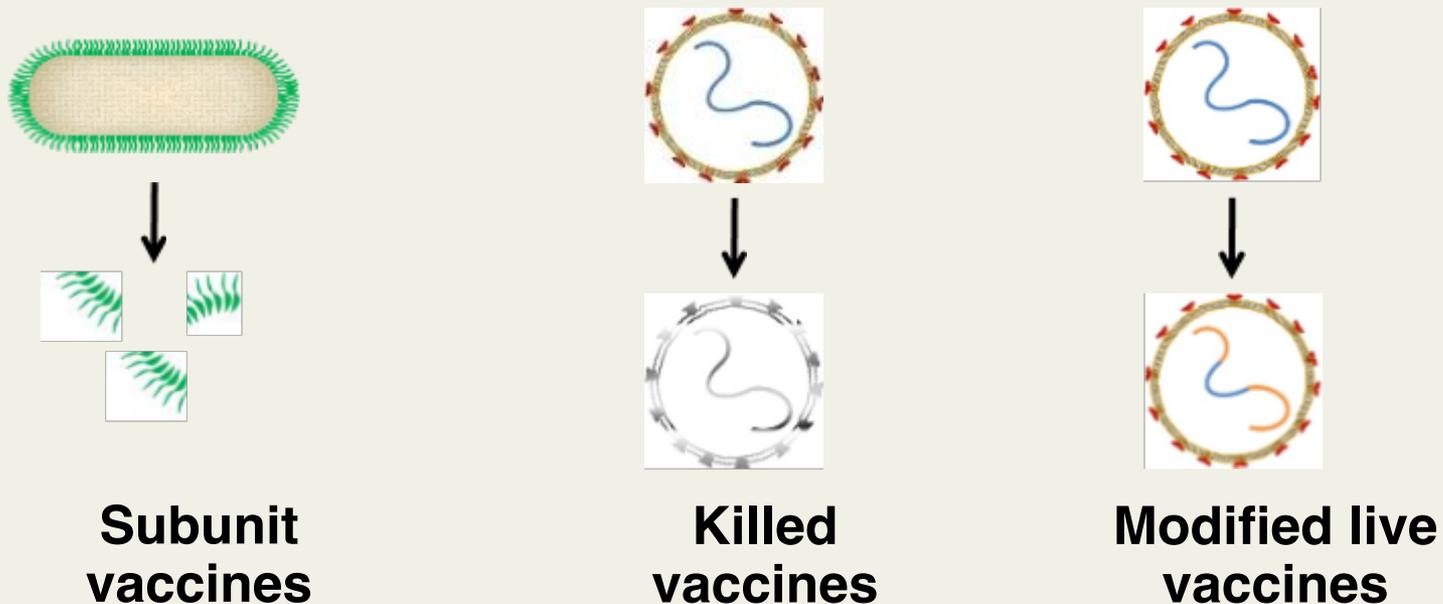
**Killed
vaccines**



**Modified live
vaccines**

How do **vaccines** work?

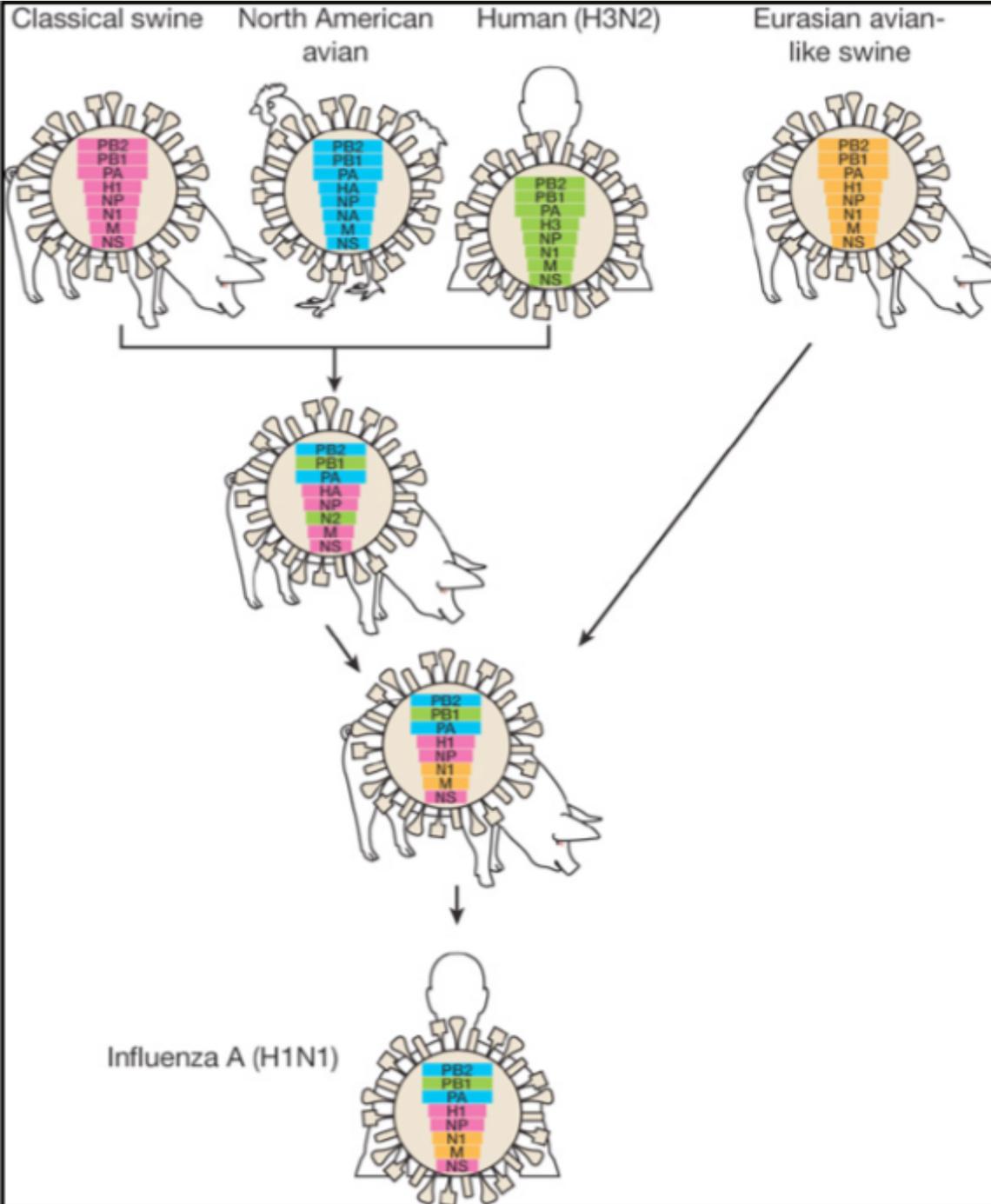
Vaccines contain non-infectious versions of a pathogen:



These incomplete or weakened versions won't make us sick, but our body will still mount an immune response against them, creating **memory B cells** in the process.

Name some diseases we are vaccinated against?

Why do we have to get the flu vaccine every year?



H1N1 Influenza Virus

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- We are protected from future infections by **memory B cells**.
- **Vaccines** are a method of creating memory B cells without causing illness.

About the Scientist:

- What do I study?
- Why do I love science?
- Questions?

