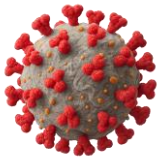
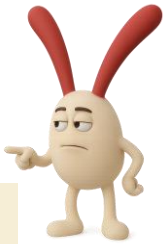
IMMUNOLOGIC MEMORY

DEFINITIONS

- **Antigen** (bad guy): Something that causes the immune system to create **antibodies**
- **Antigen Presenting Cells**: Cells that consume stuff, usually protein (antigen) and present fragments
    - Fragments are usually 13-25 amino acids long
    - B cells, Macrophages, Dendritic Cells, etc.
    - Antigen fragments are presented to **T Helper Cells**
- **Antibody**: Protein made by B cells that tags (marked for death) the bad guy (antigen)
- **Cognate Antigen**: Antigen that matches the B cell's receptors (antibodies)
- **Epitope**: Tiny part of the antigen that the antibody recognizes and attaches
    - Usually, ***6-12 amino acids***
- **Paratope**: Part of the antibody that recognizes and attaches to the epitope

KEY PLAYERS

- **Macrophage**

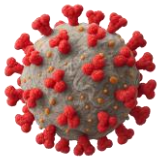
    - Recognize common molecular patterns – e.g. LPS
    - Activated by alarms (chemical signals – e.g. TNF)
    - Eats bad guys
    - Antigen Presenting Cell (APC)
    - Does not travel
    - Present in most tissues (and lymph organs/lymph nodes)
- **Dendritic Cell**

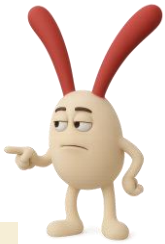
    - Recognize common molecular patterns – e.g. LPS
    - Activated by alarms (chemical signals – e.g. TNF)
    - Eats bad guys
    - Antigen Presenting Cell (APC)
    - **TRAVELS**
    - Present in most tissues (and lymph organs/lymph nodes)
- **Killer T Cell**

    - Inspect molecules from inside other cells
    - All cells are required to break up and present pieces of proteins they are making
    - Killer T Cells kill cells that present foreign pieces of proteins
- **Helper T Cell**

    - Inspect molecules from Antigen Presenting Cells (APCs)
    - Helper T Cells "help" by using chemical signals (cytokines) to direct the response
        - Type of invader
        - Defense needed
        - Location

IMMUNOLOGIC MEMORY





KEY PLAYERS (CONTINUED)

- **B Cell**
  - You make one billion B cells per day for life
  - Each cell has unique receptors (BCR) which are like attached antibodies
  - ~100,000 receptors on a single B cell – all the same
  - The variety of BCRs is diverse enough to recognize any possible organic molecule.

- ***Plasma Cell***
  - Activated B cell
  - B cell doubles in size and divides
  - 12 hours per growth and division
  - Keeps doing this for about a week
  - Results in about 20,000 identical B Cells
  - Each plasma cell makes 2,000 antibodies per second!

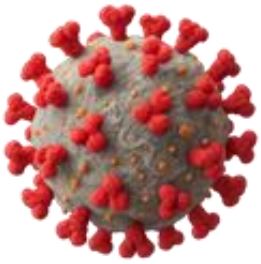
ANTIBODIES

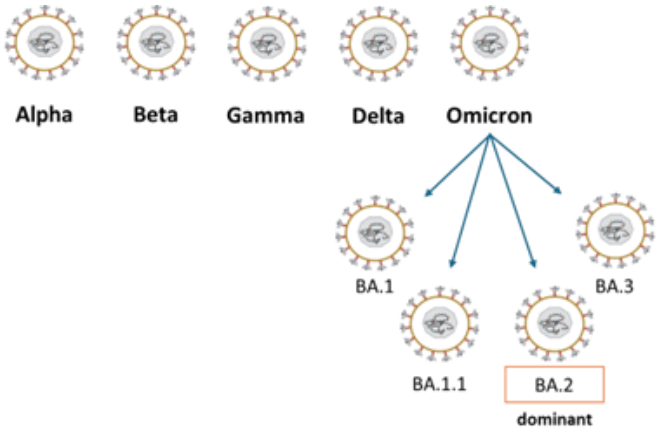
epitope

Recognizes **epitopes** that are typically:

- 5–8 amino acids (for linear/continuous epitopes) or 15–22 amino acids (for conformational/discontinuous epitopes that come together in 3D structure).
- 3–6 monosaccharide units (carbohydrate)
- 1–3 sugar residues (glycolipid)

NOTE: If the antigen (virus/bacteria) mutates, it is possible the epitope changes enough where the antibody no longer recognizes it. **COVID** is a good example:





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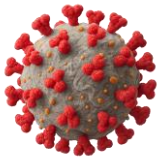
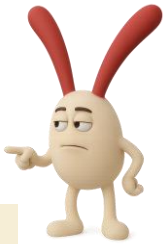
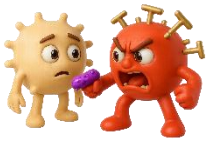
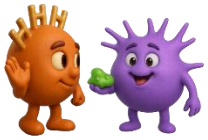



ANTIGEN PRESENTATION

All cells must chop up their proteins and present them to Killer T cells
- If it is a foreign harmful protein, the Killer T cell kills the presenting cell.




Antigen presenting cells (APCs) sample protein from their environment and present it to Helper T cells
- If it is a foreign harmful protein, the Helper T cell directs an appropriate immune response.




MEMORY

B CELL MEMORY

Short-Lived Plasma B Cells
- Produced in lymphoid follicles of secondary lymphoid organs
- Travel to bone marrow or spleen and produce massive numbers of antibodies
- Live only a few days

Long-Lived Plasma B Cells
- Travel to bone marrow
- Continually produce modest amounts of antibodies (**life-long immunity**!)
- Live a long time

Central Memory B Cells
- Memory stem cells that slowly proliferate to maintain a pool of central memory B cells
- Stand ready to produce a burst of short-lived plasma B cells

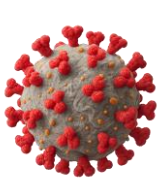
T CELL MEMORY

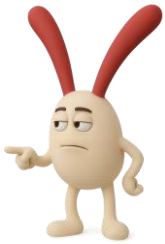
Tissue-Resident Memory T Cell
- Remain in the **tissues** near the original battle with the invader.
- Live for 10+ years

Effector Memory T Cell
- Circulate in **blood and lymph.**
- Live for 10+ years

Central Memory T Cells
- Remain in **secondary lymphoid organs.**
- Live for 10+ years

IMMUNOLOGIC MEMORY





PUBLIC HEALTH POLICY

BALANCE BETWEEN PROMOTING WELFARE AND PROTECTING LIBERTY.

"We the People of the United States, in order to form a more perfect Union, establish justice, insure domestic tranquility, provide for the common defense, ***promote the general Welfare***, and ***secure the Blessings of Liberty*** to ourselves and our posterity, do ordain and establish this Constitution for the United States of America."

Whenever the government proposes to restrict a fundamental right, it must apply the test of "strict scrutiny"

- ✓ ***Fundamental right to bodily integrity / refuse medical treatment***

STRICT SCRUTINY

- The government must show a **compelling interest;**
- The law must be **narrowly tailored and;**
- The government must use the **least restrictive means**

COMPELLING INTEREST

- A **governmental interest of the highest order** — so important that it justifies limiting a fundamental right. It's not just "important" or "convenient"; it must be **necessary to achieve an essential objective of society**.

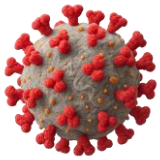
LEAST RESTRICITVE MEANS

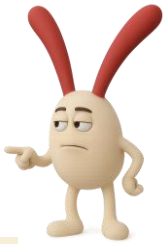
- Choosing the option that achieves the intended policy goal while imposing the smallest possible burden on people's rights, freedoms, or choices.

NARROWLY TAILORED

- A narrowly tailored policy ensures all those and only those eligible for a burden/benefit receive the burden/benefit.

IMMUNOLOGIC MEMORY



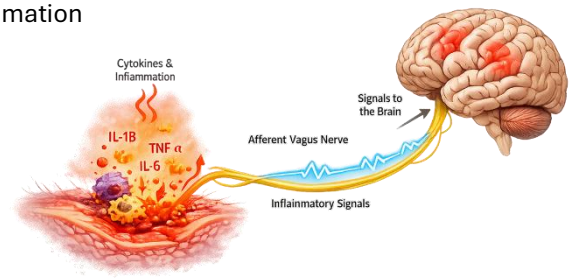


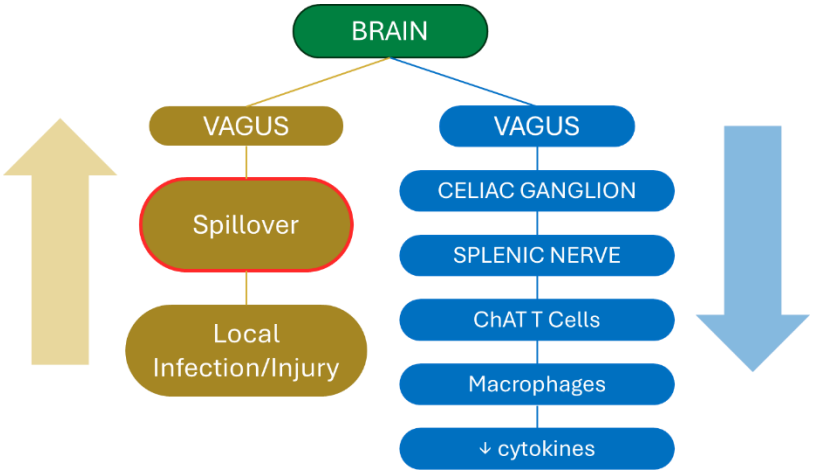
ANTI-INFLAMMATORY REFLEX

A rapid neuro-immune reflex that limits excessive inflammation

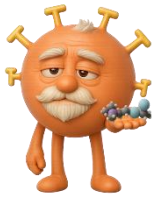
Requires **high parasympathetic tone** to be successful

Chronic low-grade inflammation kills it





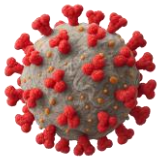
CHAT MEMORY T CELL

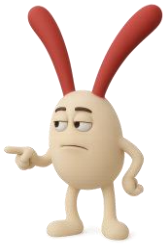


- Formed by **acute**, bounded antigen exposure
- **Transient Injury** - short-lived endotoxin exposure
- Vagal **afferent sensing** of inflammation
- Sympathetic splenic nerve firing
- **Pulsatile** β_2 signaling → *induces ChAT*
- Chronic catecholamines → *downregulates β_2 receptors*

- Hangs out in the **spleen**.
- Live for years/decades
- Makes **acetylcholine**
- Calms macrophages
- Cholinergic function is ***fragile***

IMMUNOLOGIC MEMORY





HIGH BASELINE INFLAMMATION DIMINISHES THIS MEMORY

A cholinergic memory T cell persists when:

- Baseline inflammation is low
- Sympathetic signaling is **episodic**, not continuous
- β_2-adrenergic receptors remain sensitive
- Mitochondrial function is preserved

A cholinergic memory T cells diminish when:

- Baseline inflammation is high
- Sympathetic signaling is chronic, continuous
- β_2-adrenergic receptors become insensitive
- Mitochondrial function is diminished

These cells fail when the nervous system asks them to act too often, for too long, in the wrong context. What causes chronic baseline inflammation:

Glycation

Visceral Adipocity

Leaky Gut

INFLAMMATION

"Those who can make you believe absurdities can make you commit atrocities."- Voltaire