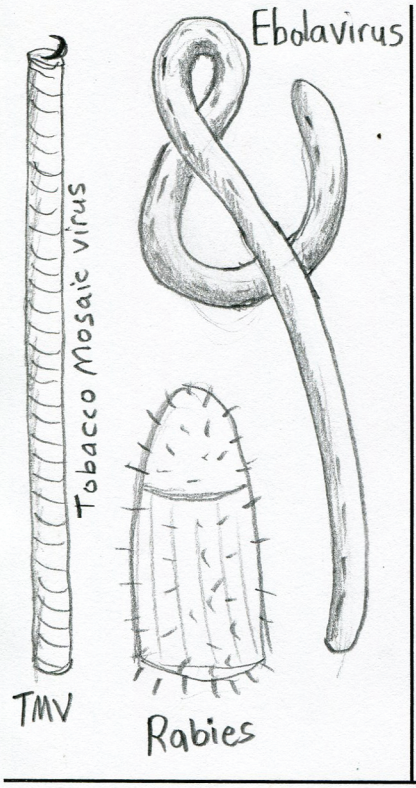
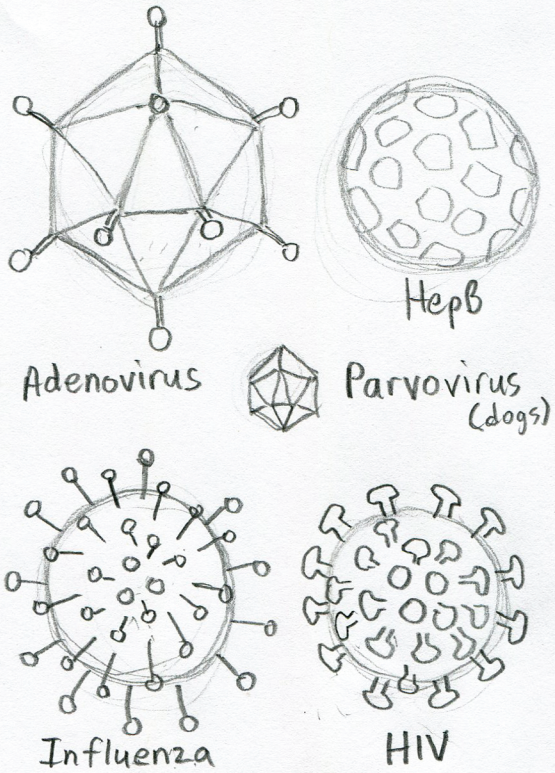
# 1: VIRUS MORPHOLOGY and ANATOMY

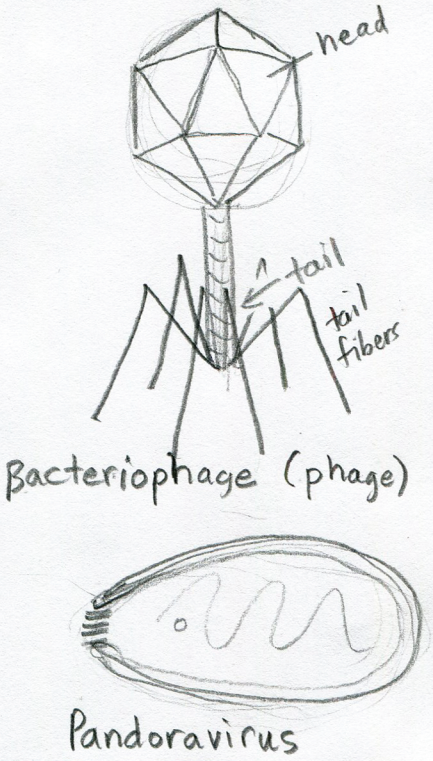
**RODS** ("Helices")



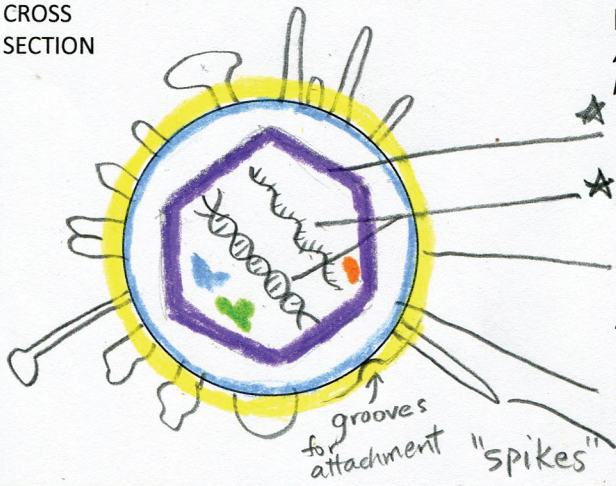

**ICOSAHEDRONS** (includes spheres)




**COMPLEX** shapes




CROSS SECTION

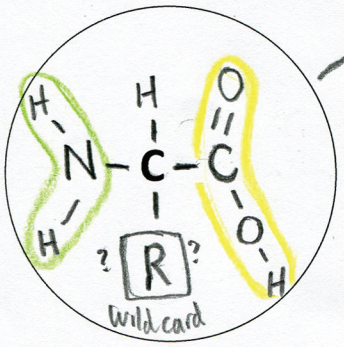



**POSSIBLE PARTS** of an ICOSAHEDRAL virus

*All viruses have the first two. The others are options that might be present. There are also lots of variations within each option!*

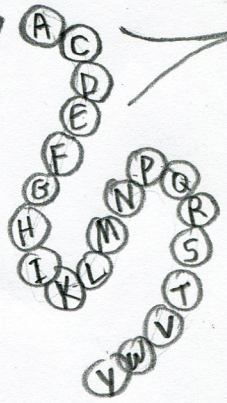
1) capsid (shell made of protein)
2) genome DNA RNA (genetic material with instructions)
3) envelope (made of lipid [cell] membrane)
4) proteins (needed for making messenger RNA)
5) matrix (a bit of extra protein under envelope)
6) glycoproteins (for attaching to cell)

**WHAT IS PROTEIN?**



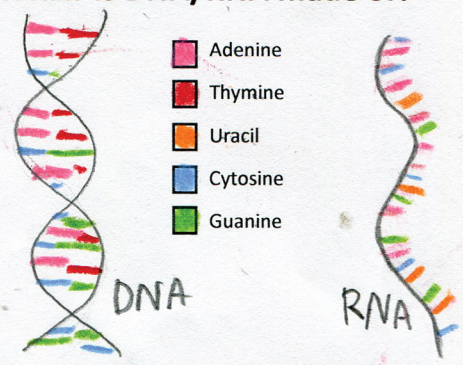

The basic unit of protein is the amino acid. It is made of atoms, but the shortcut is to draw a circle.

A long chain of amino acids is called a polypeptide.




The polypeptide folds up to become a structural protein.

**WHAT is DNA/RNA made of?**




The sides are made of ribose and phosphate.
The rungs are made of nucleid acid bases.
DNA: Adenine, Thymine, Cytosine, Guanine
RNA: Adenine, Uracil, Cytosine, Guanine

# 2(a): VIRUS SIZE

**At this scale, how big would we have to draw these things?**

a red blood cell = large truck tire

a skin cell = UPS truck

a paramecium = house

this dot • = football field

What would be too small to draw?

atoms, small molecules

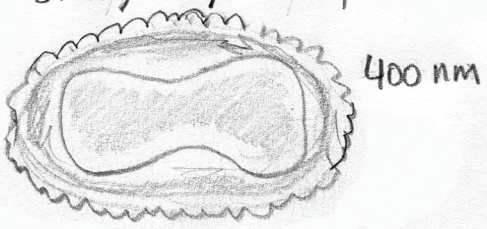
We might be able to draw DNA as a very thin line:

There are 1,000 millimeters (mm) in a meter (m).

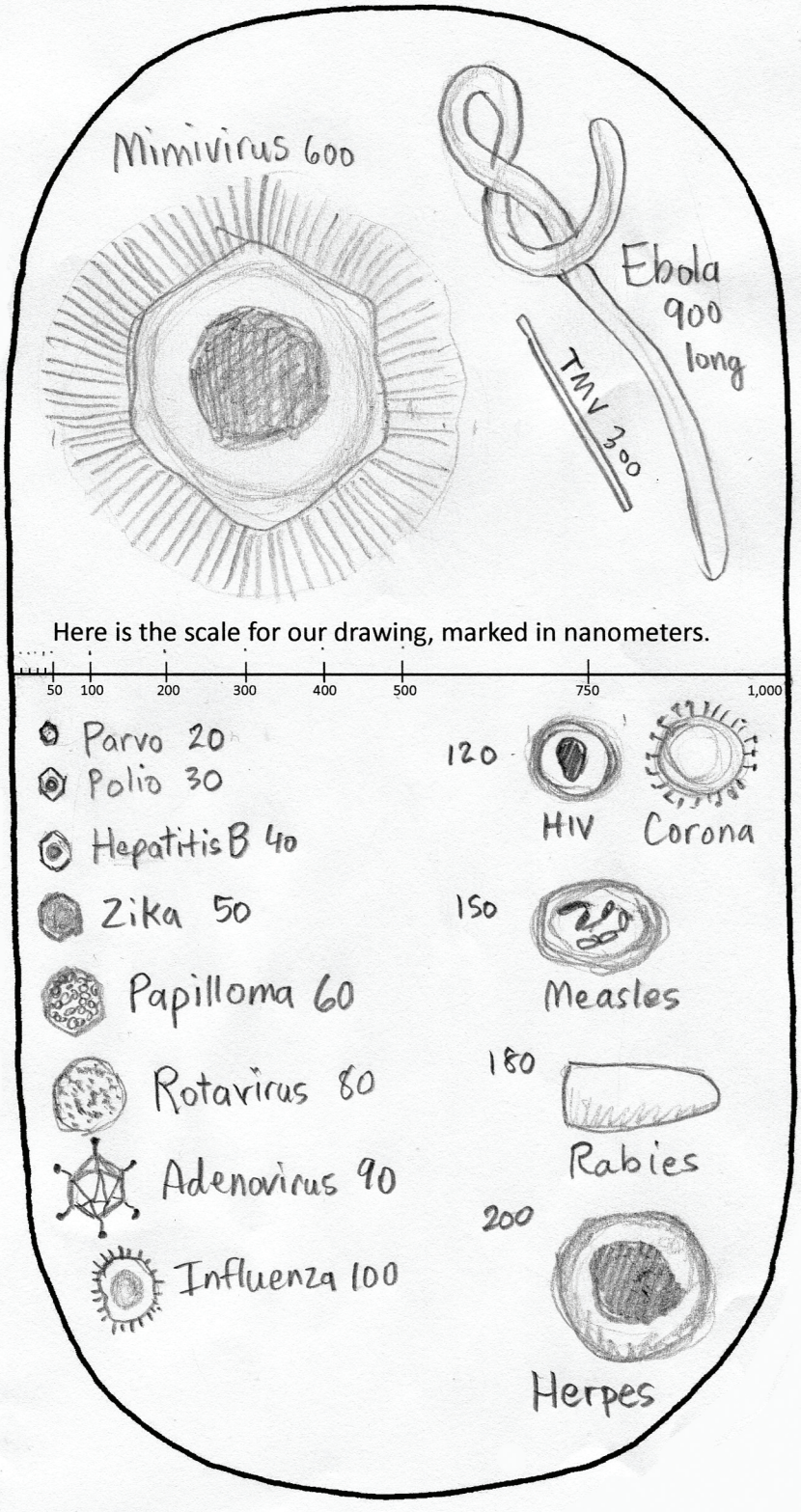
There are 1,000 microns (μ) in a millimeter (mm).

There are 1,000 nanometers (nm) in a micron (μ).

**This long, oval shape represent a bacillus bacterium.**

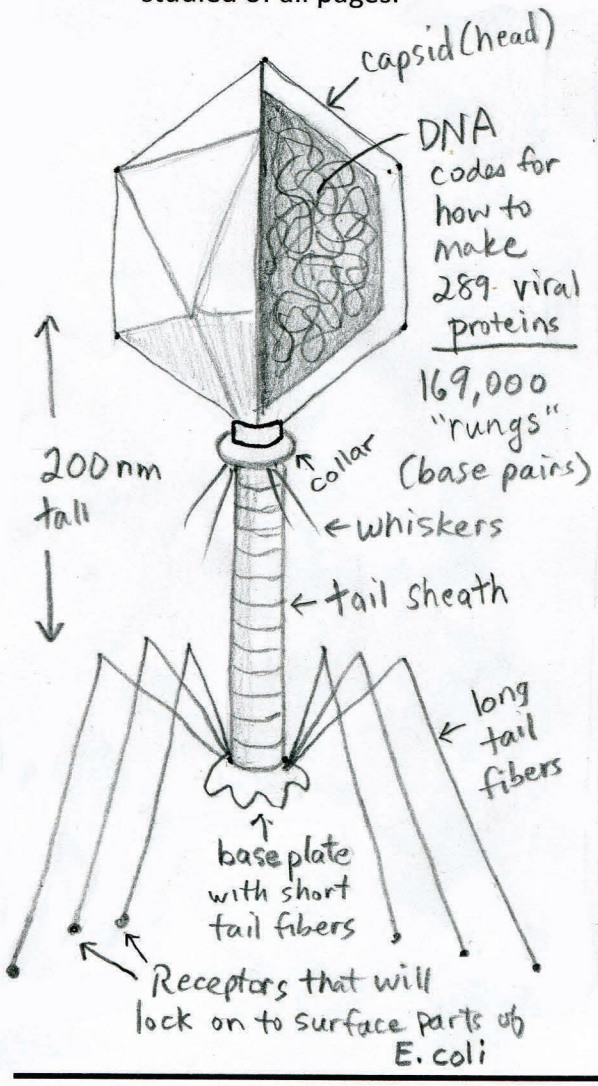




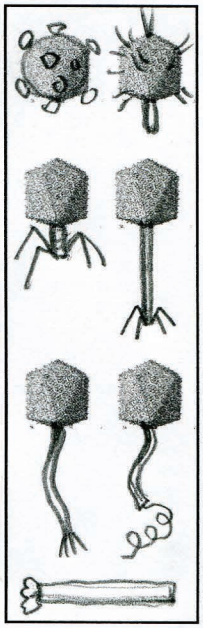


# 4(a): BACTERIOPHAGES

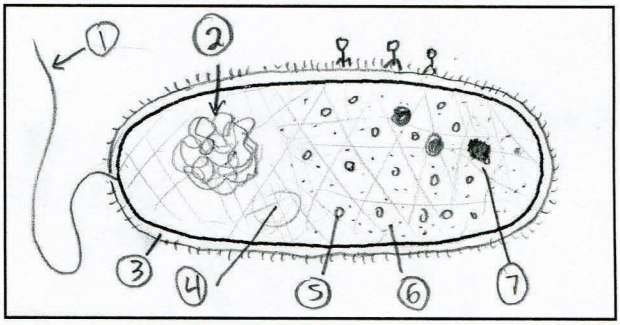
**T4** is perhaps the most studied of all pages.



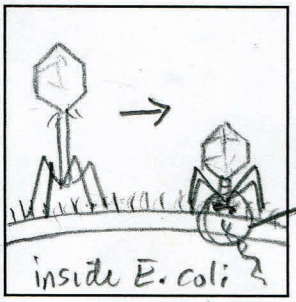

OTHER PHAGE MORPHOLOGIES



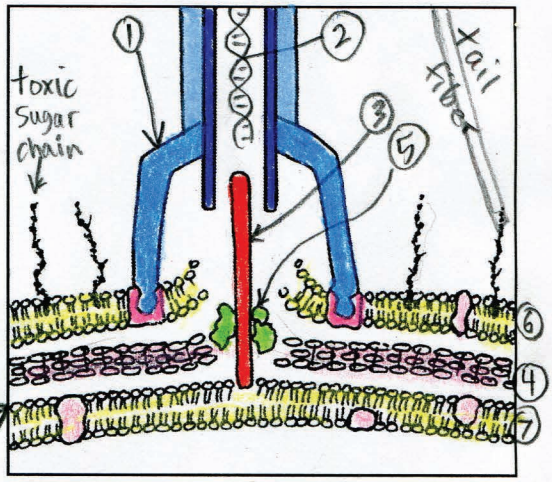
T4 attacks *Escherichia coli (E. coli)* bacteria




**(1)** flagellum **(2)** Bacterial "nucleoid" made of DNA
**(3)** cell envelope made of membrane and wall
**(4)** cytoskeleton framework that gives shape to the cell
**(5)** ribosomes **(6)** enzymes (little task "robots")
**(7)** includsions (viral production sites)




The tail sheath contracts and injects the DNA into E. coli




**(1)** Baseplate **(2)** DNA **(3)** protein "needle"
**(4)** peptidoglycan (sugars held together by proteins)
**(5)** lysozymes to digest the peptidoglycan layer
**(6)** outer membrane **(7)** inner membrane

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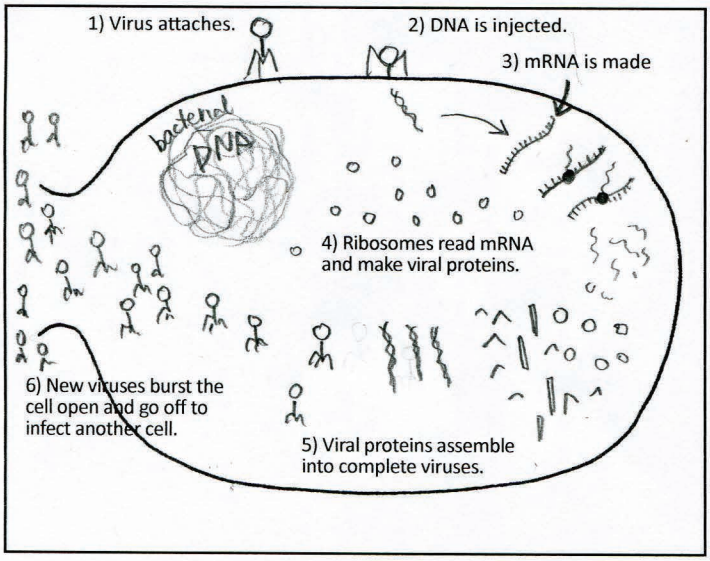
Phages have two life cycle options: **lytic** or **lysogenic.**

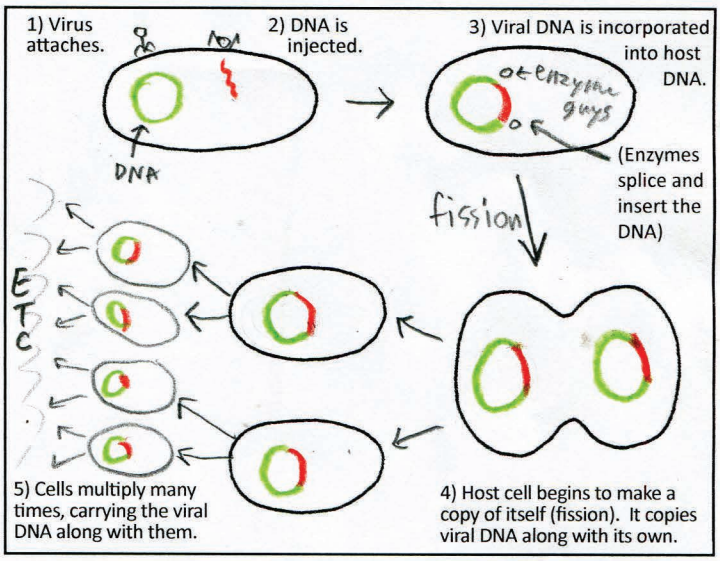
## LYTIC (causes bacteria to burst)

The virus replicates quickly (30 minutes) and then causes the cell to burst, releasing 100-150 new viruses. New viruses infect more cells.




## LYSOGENIC (hides in bacteria's DNA)

The viral DNA is incorporated into the bacteria's DNA, so when the bacteria reproduces by fission, the viral DNA is also copied.

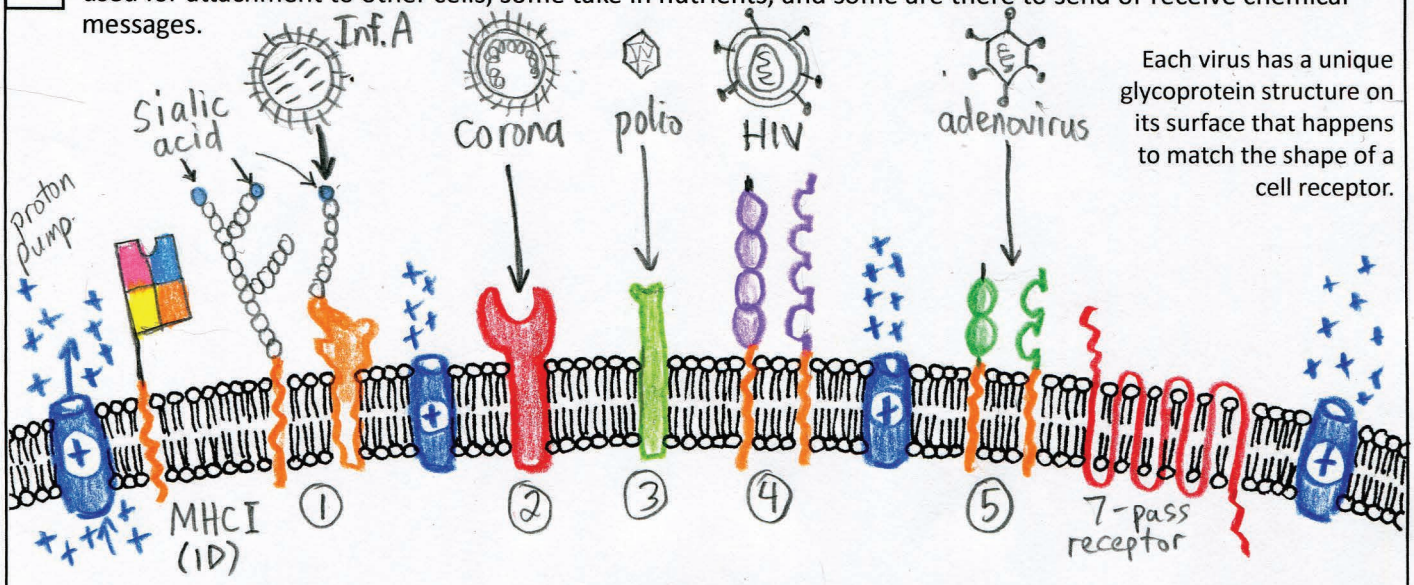


# 5(a): HOW VIRUSES ENTER CELLS

There are three steps to the entry process. All viruses do (1) and (2). Viruses with envelopes must also do (3).
**1) Attach** **2) Release genome into cells** **3) Merge viral envelope with cell membrane**

## 1

The surface of all cells is covered with a "forest" of receptors. Some are used to identify the cell, some are used for attachment to other cells, some take in nutrients, and some are there to send or receive chemical messages.



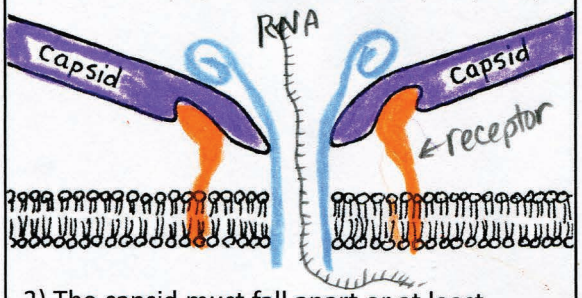

Each virus has a unique glycoprotein structure on its surface that happens to match the shape of a cell receptor.

1) Sialic acid : a tiny sugar found on the end of many long chains, especially on respiratory system cells
2) ACE2 : an enzyme that tells blood vessels to relax, found in lungs, heart, blood vessels, intestines
3) CD155 aka PVR : used to connect to other cells, found mostly in epithelial cells (skin, lungs, intestines)
4) CD4 : a receptor found on T cells to communicate with macrophages (both are white blood cells)
5) CAR : Coxsackie-Adenovirus Receptor is necessary for proper formation of the heart, and attaches cells to cells

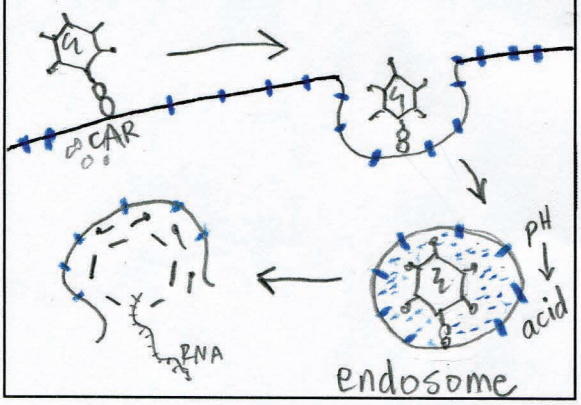
## 2

The virus must release its genome.
(Exception: Reoviruses)

1) A pore can open in the capsid. (EX: polio)



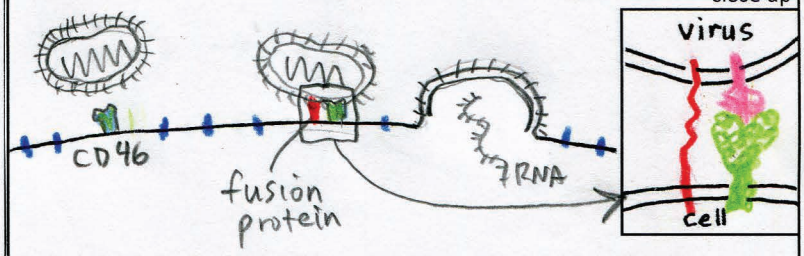

2) The capsid must fall apart or at least become very leaky (EX: adenovirus)



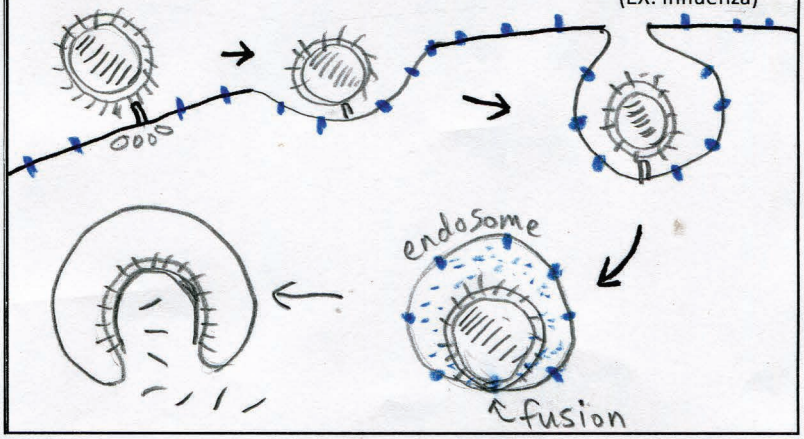

## 3

The viral envelope uses a "fusion protein" to merge with the host cell membrane.

1) Fusion occurs at the surface. (EX: HIV and measles)

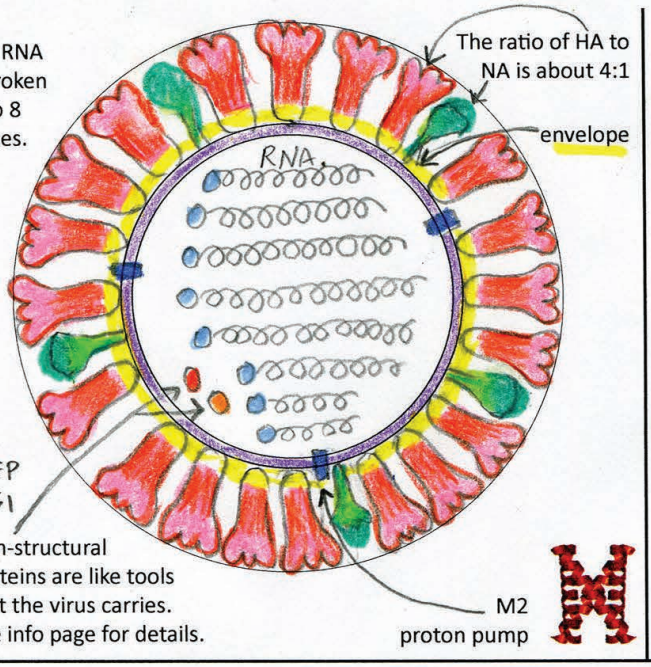



2) Fusion occurs after the virus is brought inside the cell.
(EX: Influenza)

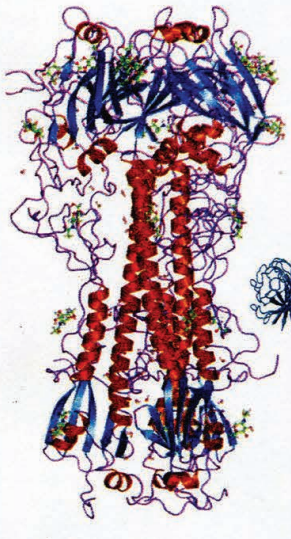


# 5(b): HOW INFLUENZA ENTERS CELLS

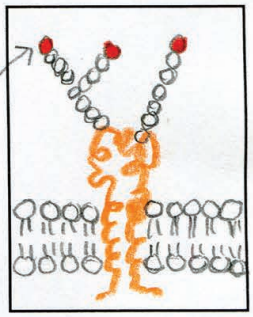
Influenza A is one of the most studied viruses of all time. Its binding site, sialic acid, was the first virus receptor to be discovered (1985). Its genome and its glycoprotein structures have been completely mapped.




"Spikes" are a type of glycoprotein. (Glyco = sugar)



The HA head has a "pocket" that can bind to a sialic acid.

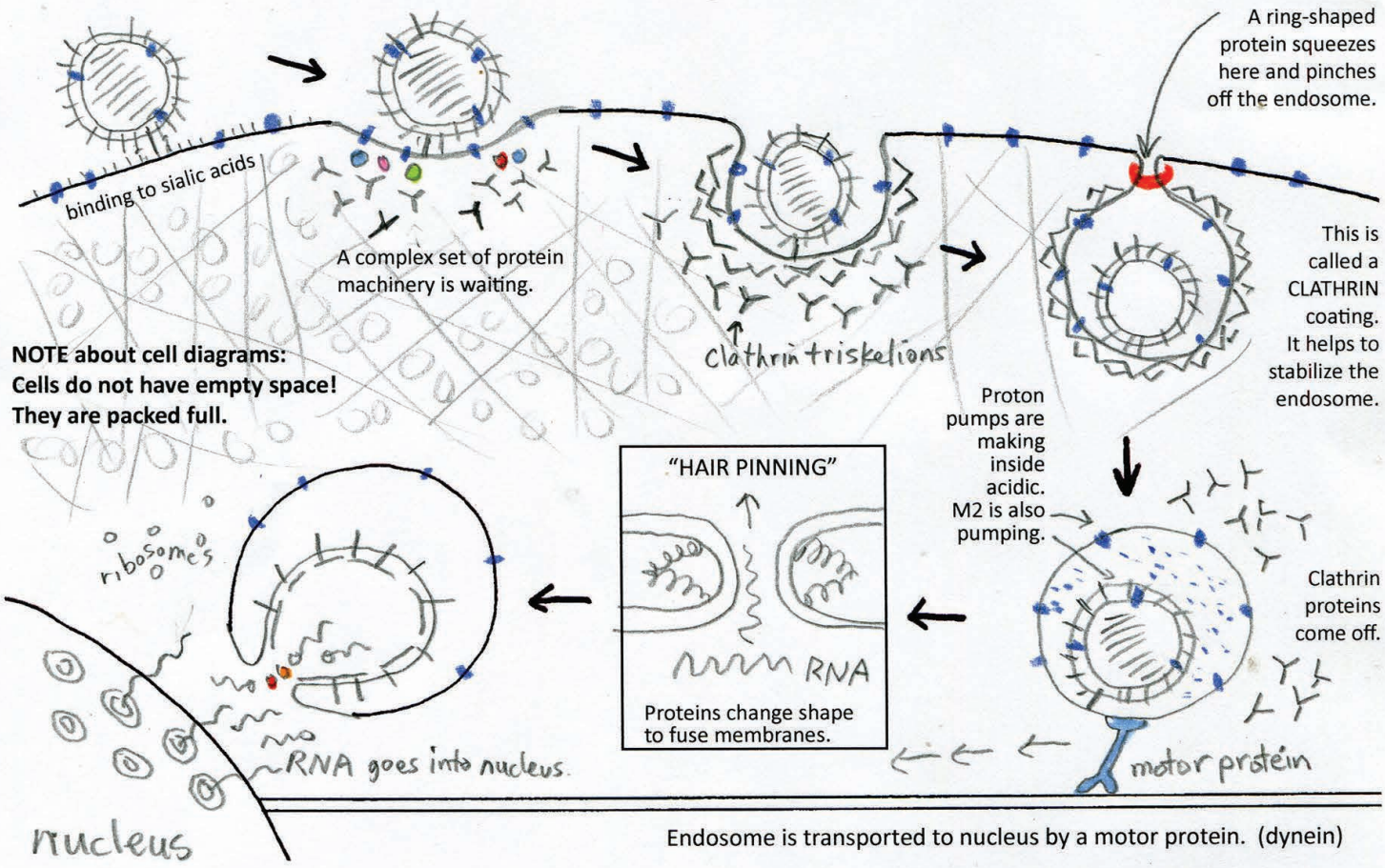


NA Neuraminidase is a "snipping enzyme" that cuts off (cleaves) sialic acid molecules. **(This enzyme will be needed to exit cell.)**

HA Hemagglutinin (heme= blood, agglutinate= clump)

Influenzas are named according to the structure of their HAs and NAs. As the virus replicates (billions upon billions of times) small changes occur. The first variations that were mapped were called H1 and N1. (This corresponds to the flu pandemic of 1918.) As more variations were found, they were named by number (H2, H3, H4, etc.).

## HOW THE INFLUENZA VIRUS IS TAKEN INTO CELLS

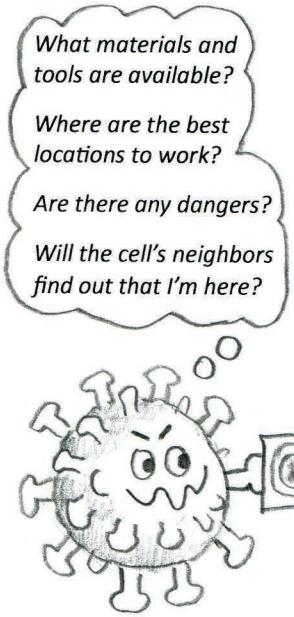



**NOTE about cell diagrams:**
**Cells do not have empty space!**
**They are packed full.**

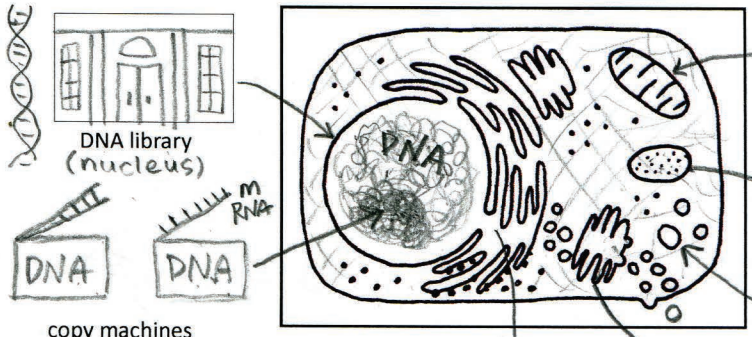
Endosome is transported to nucleus by a motor protein. (dynein)

# 6: INSIDE A CELL

What does a cell look like from a virus's viewpoint?




CELL "MAP" showing organelles




## RAW MATERIALS

*Most structures in our environment are made from metal, glass, plastics, and plant fibers. Cells have 4 basic materials that all their stuff is made of.*

0) $H_2O$, $O_2$, salts

1) amino acids

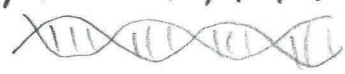
2) sugars

3) lipids (fats) carbon atoms

4) nucleoTides


## INSTRUCTIONS

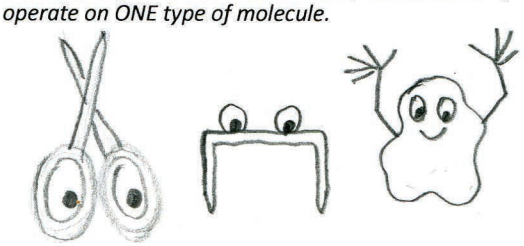
1) DNA (A,T,C,G)



2) RNA (A,U,C G)

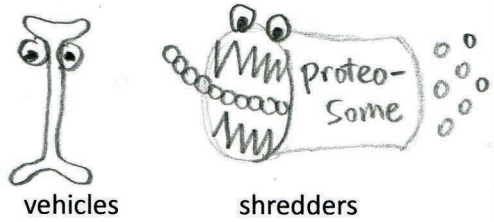
## TOOLS/"TASK ROBOTS" (need energy)

*They are usually made of protein but can have one of the other ingredients mixed in. Tools/robots can only operate on ONE type of molecule.*

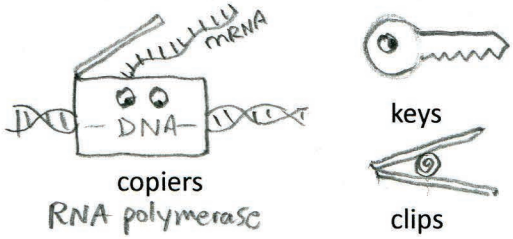


scissors staplers folders

editors (spell checkers) fixers pumps




vehicles shredders




copiers
RNA polymerase

keys

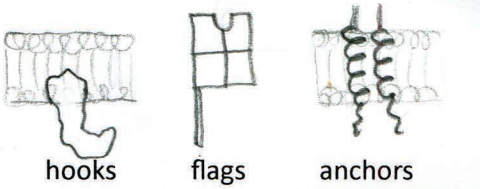
clips

## STRUCTURES

*Not all cellular structures are similar to the structures in our own environment but a surprising number are.*

cables microtubules

string actin



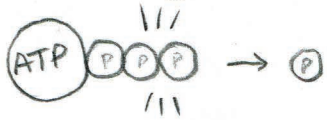
hooks flags anchors

mailboxes letters labels

**LIPID**

walls (membrane) bags vesicles tubes (ER)

**The energy to run these tools comes from the cell's "rechargeable batteries."**

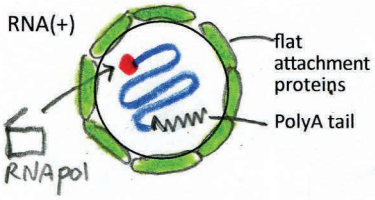



Energy is released when the third phosphate is popped off. Energy is needed to put it back on.

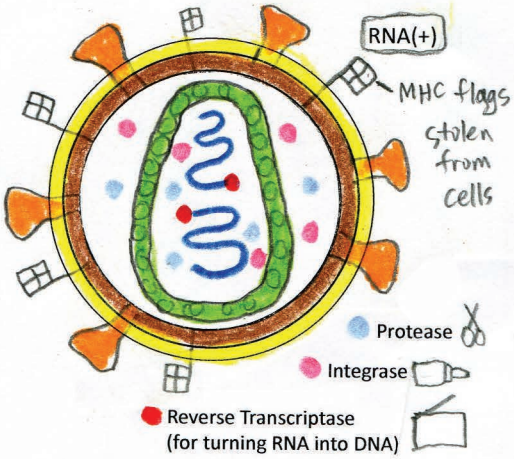
# 7(a): INSIDE A CAPSID

All viruses have a genome, which can be either DNA or RNA.
Many viruses also have one or more protein "tools" inside the capsid (tools it will need immediately after entry).

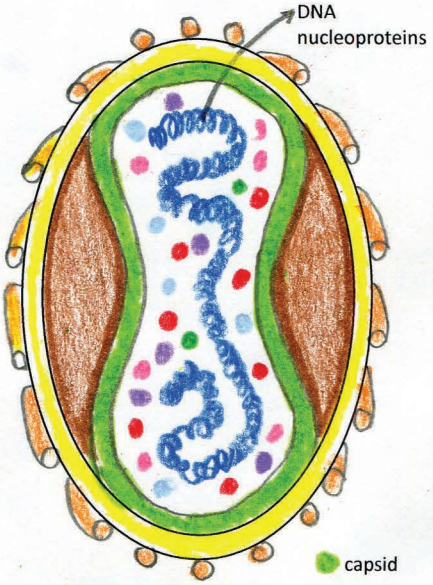
**POLIO**



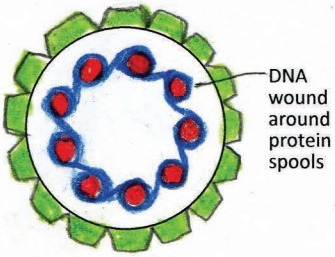

**HIV-1**



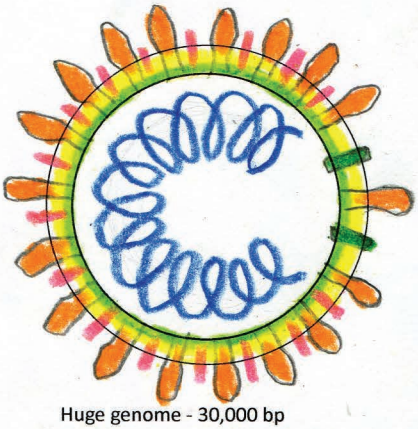

**SMALLPOX**




**PAPILLOMA** (warts)

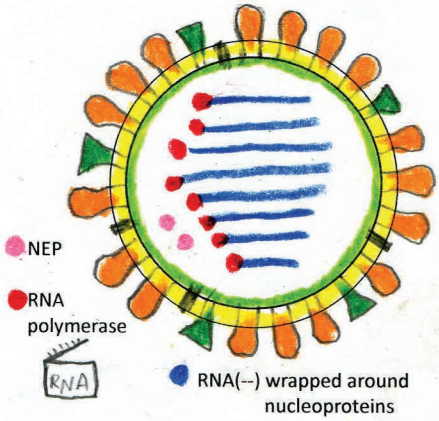



**CORONA**



Huge genome - 30,000 bp
RNA(+) is wrapped around nucleoproteins

**INFLUENZA**




**Viruses do not have:**

1) Ribosomes
2) Raw materials
3) Source of energy

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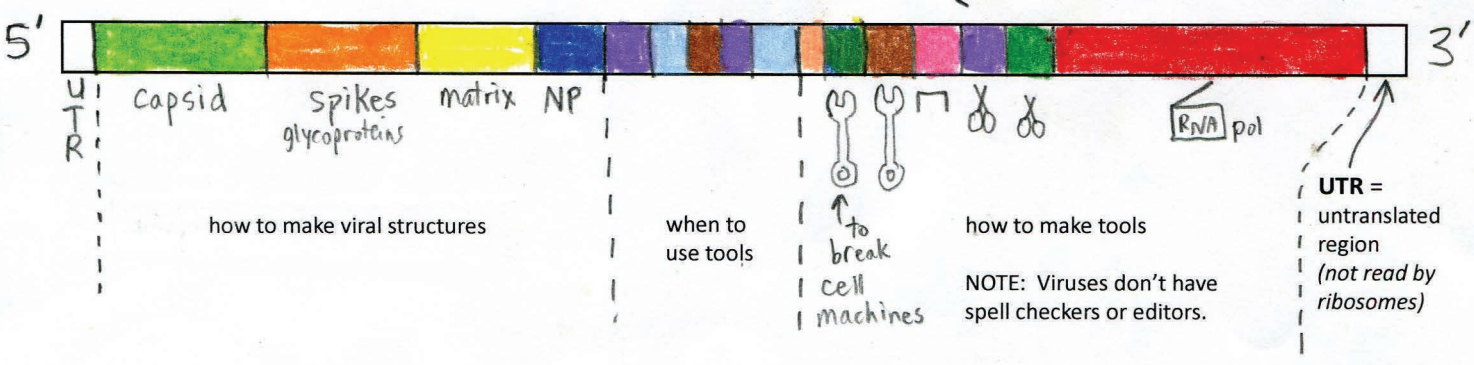
Virologists draw viral genomes as a straight line when they want to show where information is located.
Each segment represents the instructions for one thing, sort of like a chapter in a book.

Both RNA and DNA are directional.
One end is called 5-prime and the other is 3-prime.

As a general rule, the genome is read and used in this direction.



# 8(a): HERPES SIMPLEX-- A DNA VIRUS

Herpes simplex viruses (HSV) include: HSV-1, HSV-2, Varicella zoster (chickenpox), Epstein-Barr virus, and cytomegalovirus (HCMV).

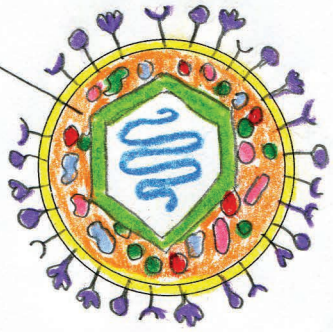
DNA genomes have 120,000 to 240,000 base pairs.

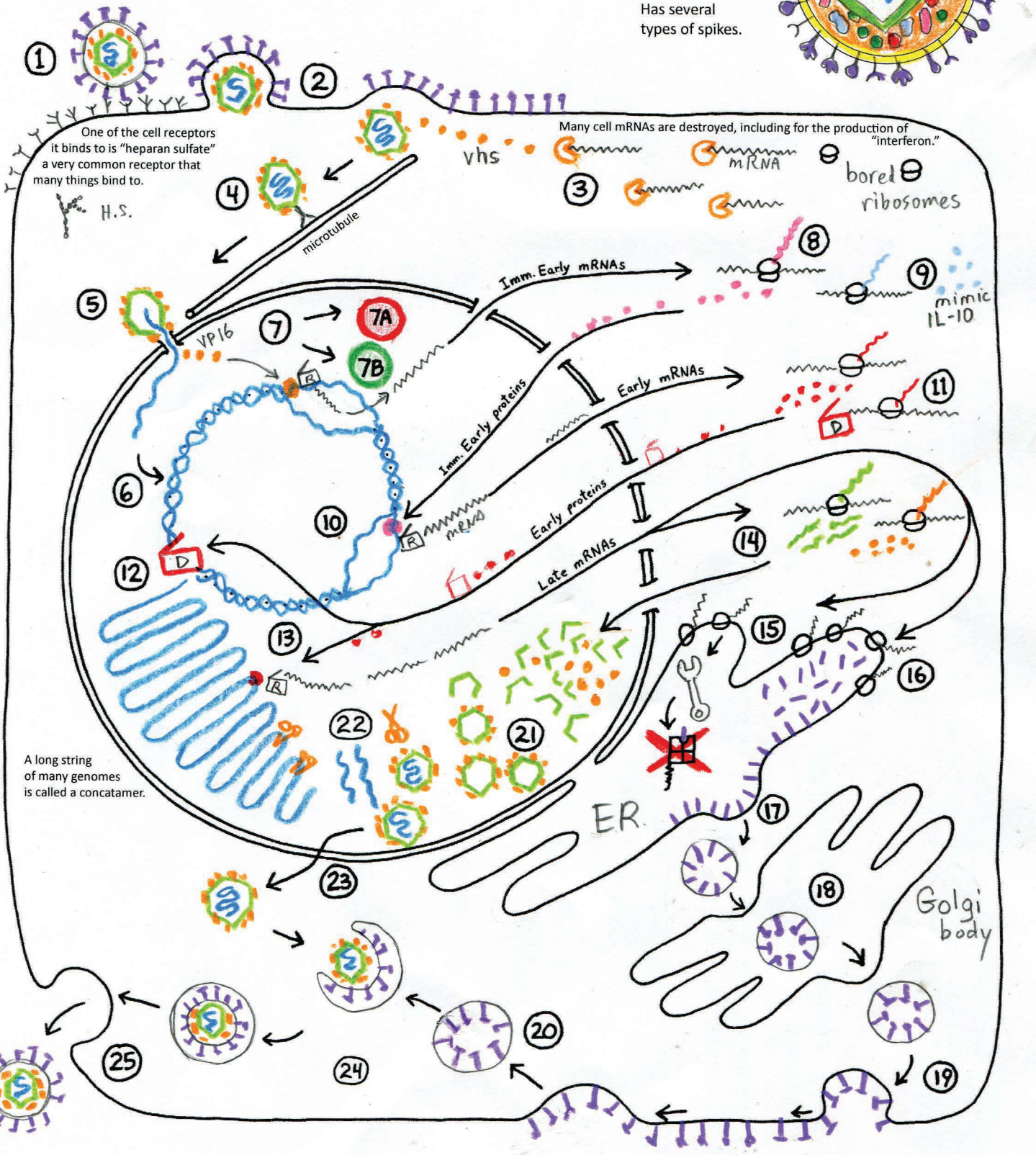
capsid
glycoproteins
tegument proteins
DNA
mRNA:

**HERPES VIRION** (150-200 nm)

Some tegument proteins will help capsid get through membranes.

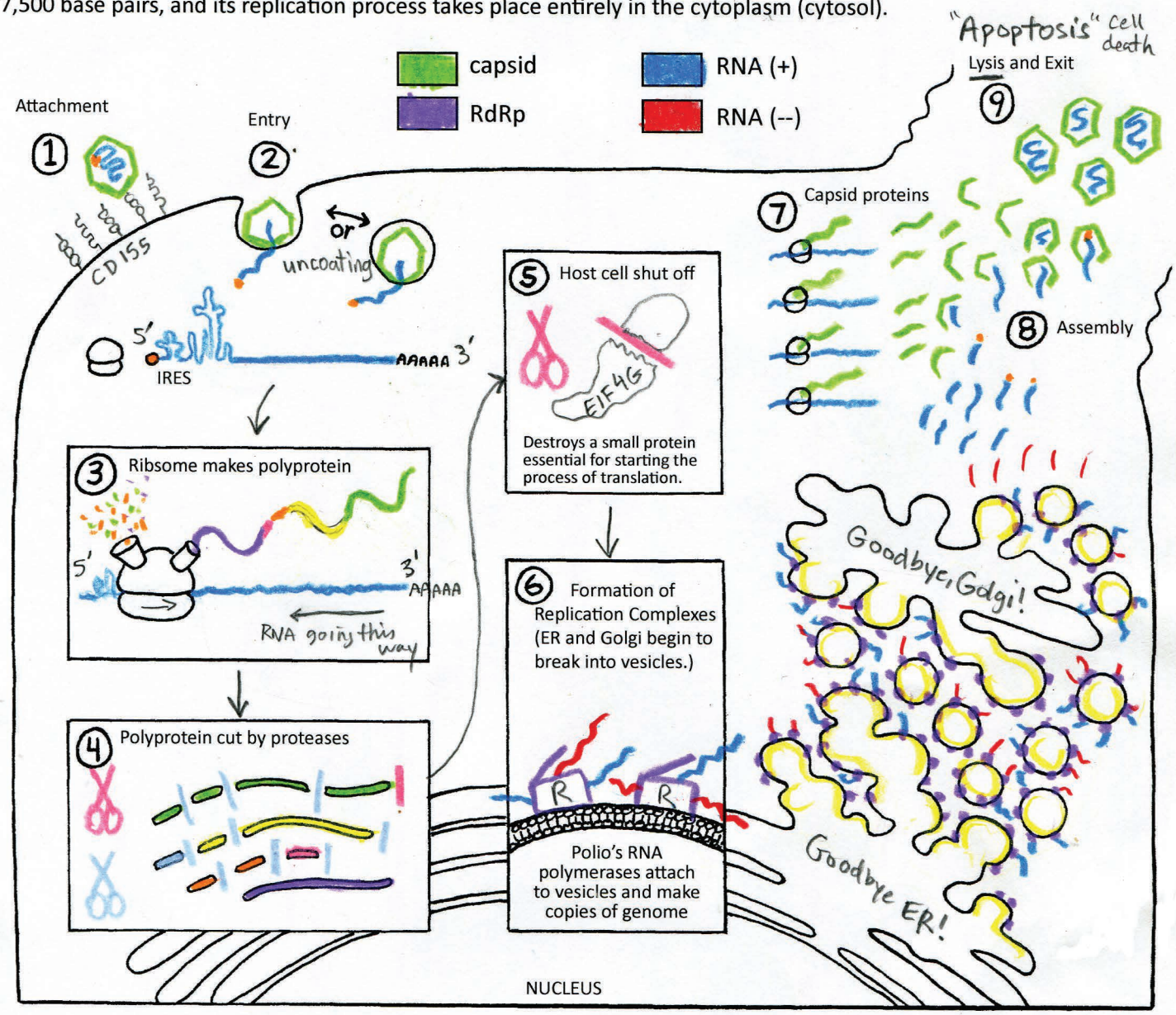
Has several types of spikes.





# 8(b): POLIO-- AN RNA VIRUS

Poliovirus is a positive sense RNA virus and is a member of the Picorna family of viruses. Its genome contains about 7,500 base pairs, and its replication process takes place entirely in the cytoplasm (cytosol).




This cell would be an epithelial (surface) cell in the intestines. After infecting many intestinal cells, the viruses will go into the blood and then make their way to nerve cells, especially motor neurons in the spine.

NOTE: It takes two rounds of copying to get a (+) sense strand for the capsids.

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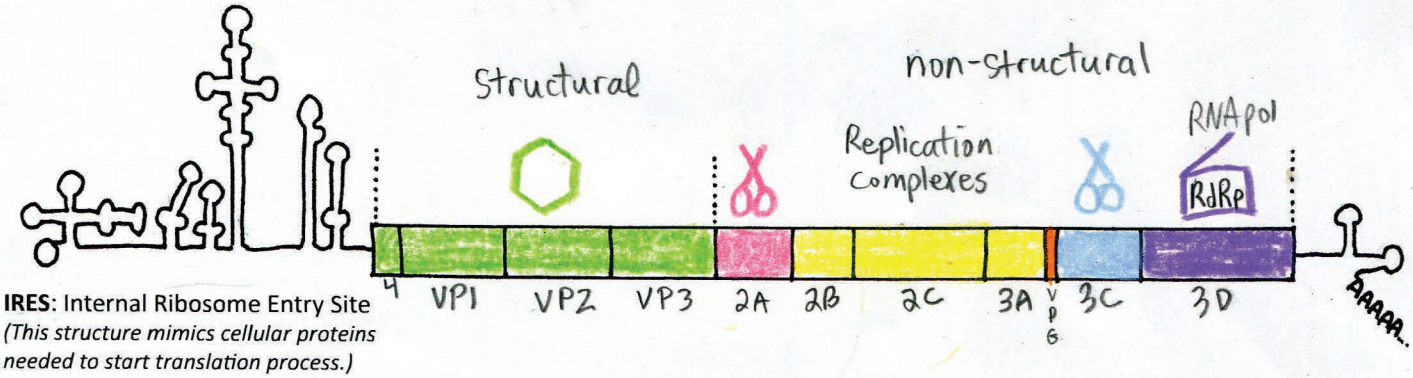
This is how virologists draw the polio genome. They like to show the IRES, but also like to use a line to show genes.




**IRES**: Internal Ribosome Entry Site
*(This structure mimics cellular proteins needed to start translation process.)*

# 9: THE BODY FIGHTS BACK

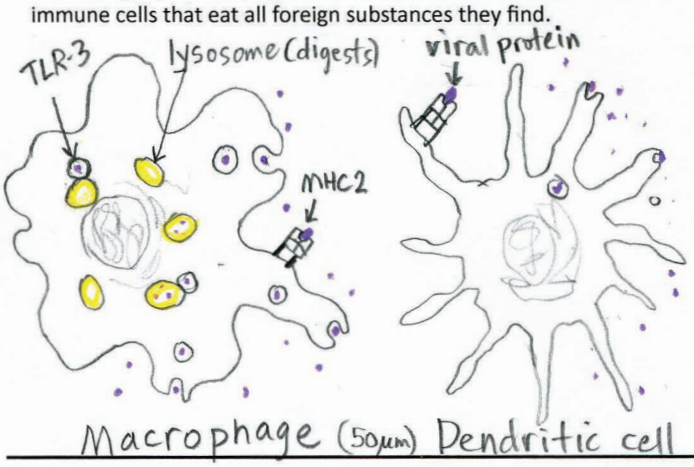
This lesson is not a complete overview of the immune system. We'll focus on the fight against viruses, although much of this information would apply to other pathogens as well. The body has several layers of defense. Most viruses are kept out because of physical barriers, but if some get past those, we have two more levels of defense: the **innate** (non-specific) immune system, and the **adaptive** (specific) system.

## 1) PHYSICAL BARRIERS

These work so well that under normal circumstances we go about our lives oblivious to the vast number of viruses in our environment.

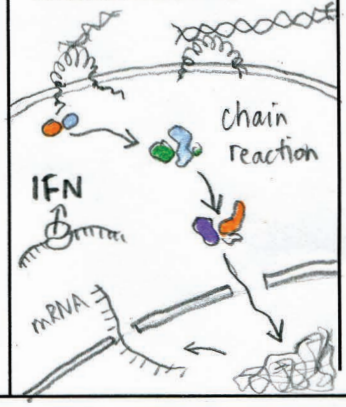

## 2) ROAMING "EATERS" (phagocytes)

If viruses get past our physical barriers, they are met by roaming immune cells that eat all foreign substances they find.




## 3) SENSORS that detect viruses

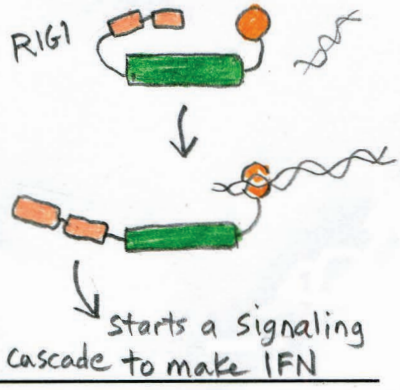
**TLR-3** Found on the outside of phagocytes, and inside their endosomes.




**EXAMPLES:**

**RIG-1** **MDA-5**

Found in the cytoplamsm of all cells. They detect viral RNA (usually dsRNA).

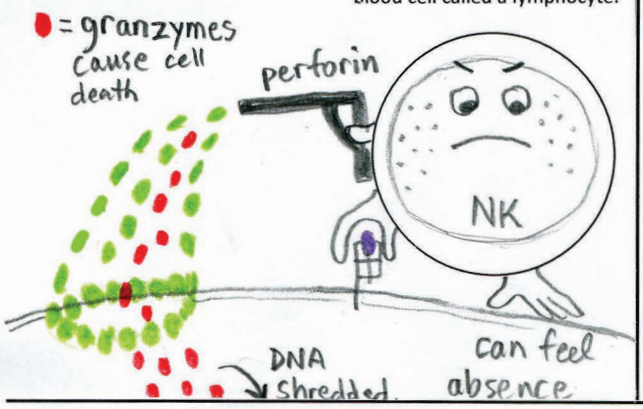



## 4) INTERFERON

The sensors trigger the production of interferon, a chemical message that causes the production of many anti-viral proteins, and also alerts other cells to the presence of the virus.

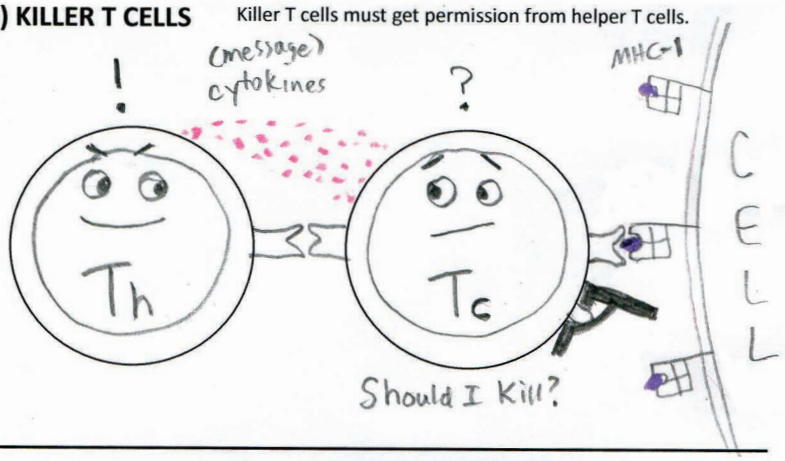
## 5) NATURAL KILLER CELLS

NK cells are a type of white blood cell called a lymphocyte.

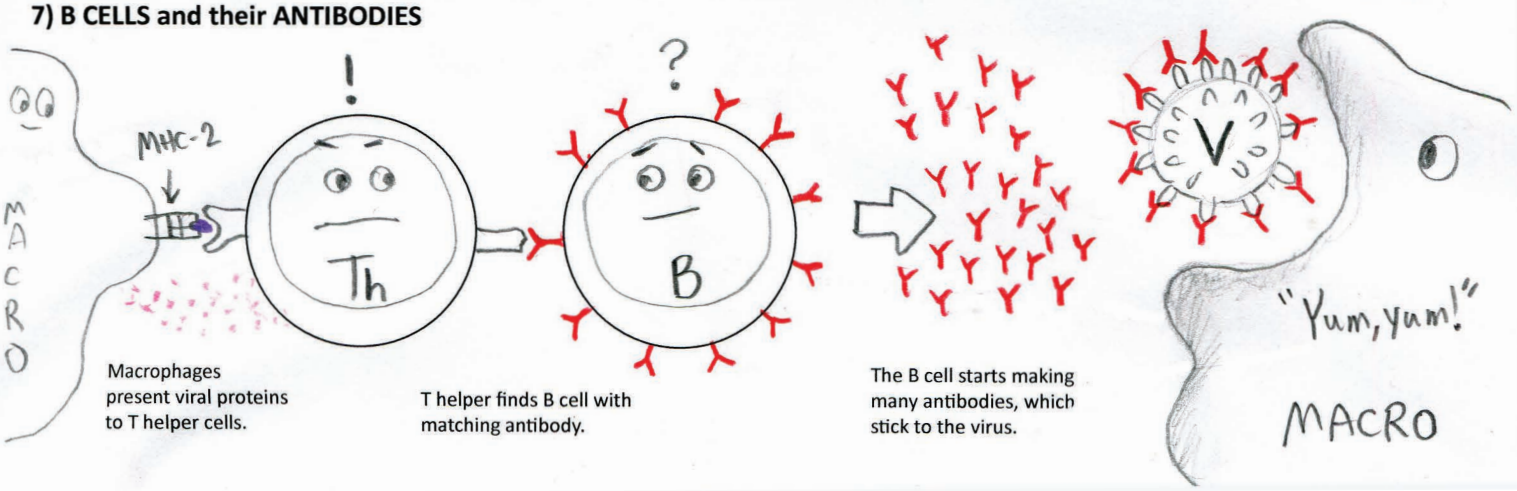



## 6) KILLER T CELLS

Killer T cells must get permission from helper T cells.




## 7) B CELLS and their ANTIBODIES



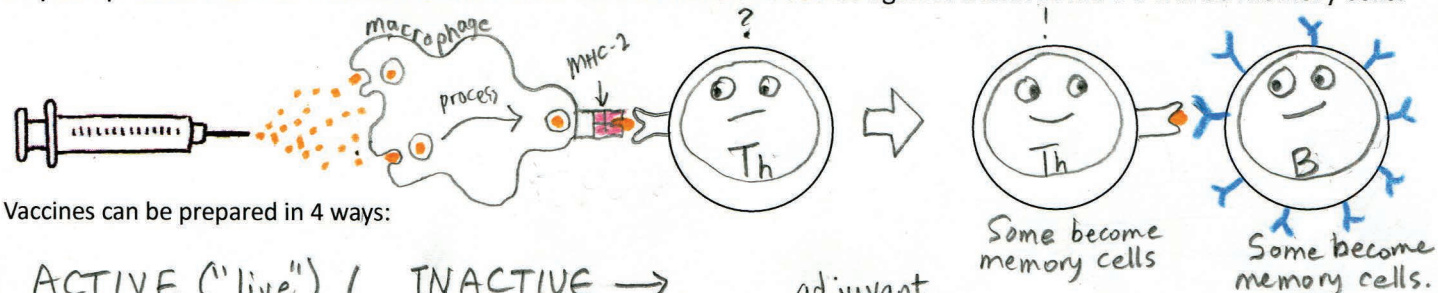

Macrophages present viral proteins to T helper cells.

T helper finds B cell with matching antibody.

The B cell starts making many antibodies, which stick to the virus.

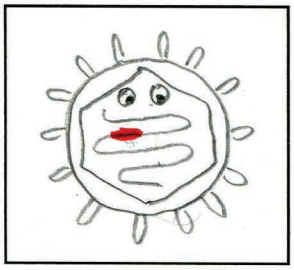
# 10: VACCINES and ANTI-VIRALS

**VACCINE:** The goal is to imitate an infection by giving the macrophages viral antigens (either parts or whole) so they can present them to T cells who then tell B cells to make antibodies against them. Some B's will be memory cells.




Vaccines can be prepared in 4 ways:

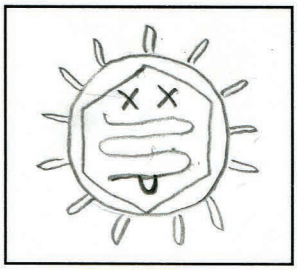
ACTIVE ("live") | INACTIVE →



1) Attenuated

The genome has mutated so the virus can't cause illness. Virus retains some ability to replicate.

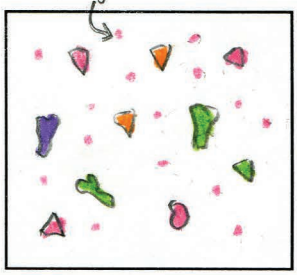
EX: oral polio (Sabin), y.f. M, M, R, chickenpox



2) Whole virus

The virus has been treated with chemicals to "kill" it, but the T cells still recognize the proteins.

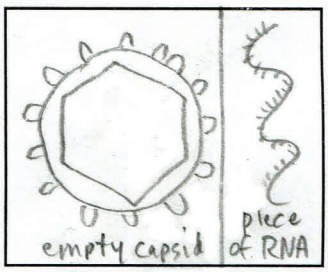
EX: injected polio (Salk), Hep A, rabies




3) Fractional

Only small parts of the virus are used, such as a piece of the spike, or one capsid protein.

EX: influenza, Hep B, papilloma (HPV)




4) Recombinant

Cloning techniques are used to make yeast cells produce either empty capsids, spikes, or strands of RNA.

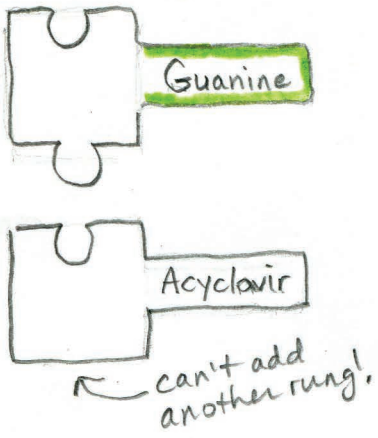
EX: influenza, Hep B, papilloma

**ANTI-VIRALS:** The goal is to block or break a viral structure without harming any host cells. This is tricky! Here are three of the most successful strategies so far (though resistance is already a problem).

**Strategy #1: Nucleoside analogue (mimic)**

These try to stop the replication of viral DNA or RNA by giving the virus a supply of fake rungs that do not have a sugar.

Ex: Acyclovir is a guanosine (G) mimic

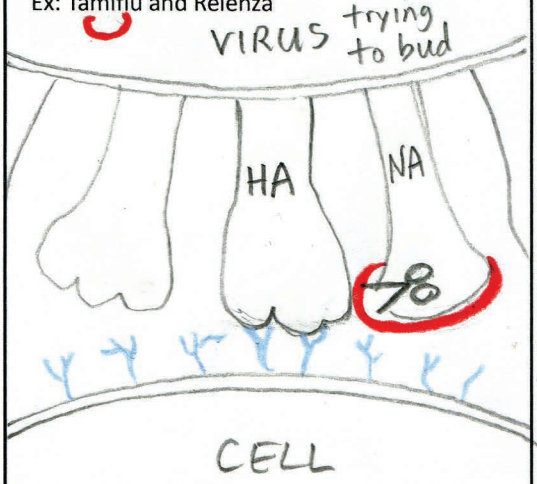



Other examples:
1) AZT (for HIV) mimics "T."
2) Remdesivir (for Ebola) mimics "A."

**Strategy #2: Block action of NA (Influenza)**

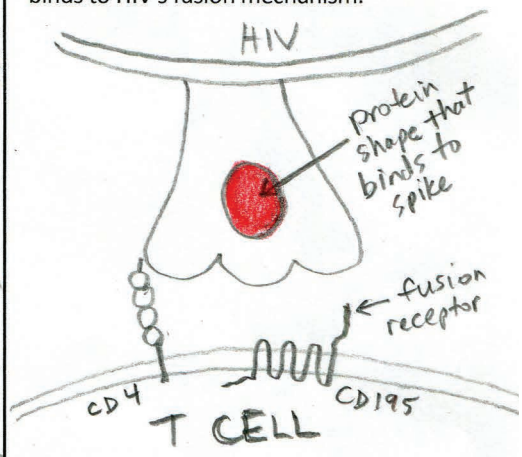
Block the snipping action of neuraminidase so influenza viruses can't bud out of cell.

Ex: Tamiflu and Relenza




**Strategy #3: Stop fusion (HIV)**

The HIV drug Fuzeon is a protein that binds to HIV's fusion mechanism.




Can't prevent attachment, but prevents fusion.

**Strategy that used to work: Block Influenza's M2 ion channel**

Influenza viruses are now resistant to Amantadine, so it is no longer used.