Immunological memory and Vaccines

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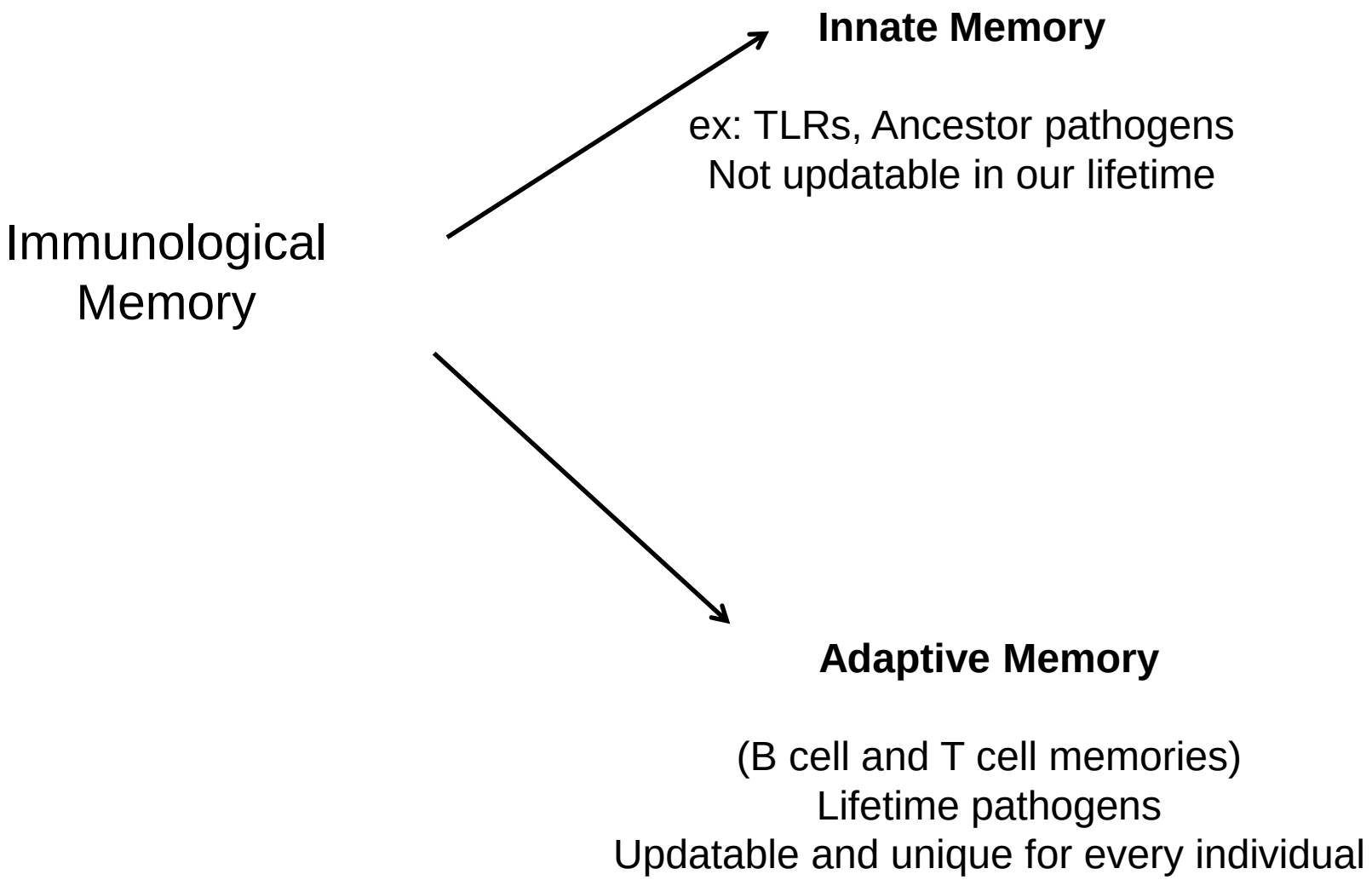
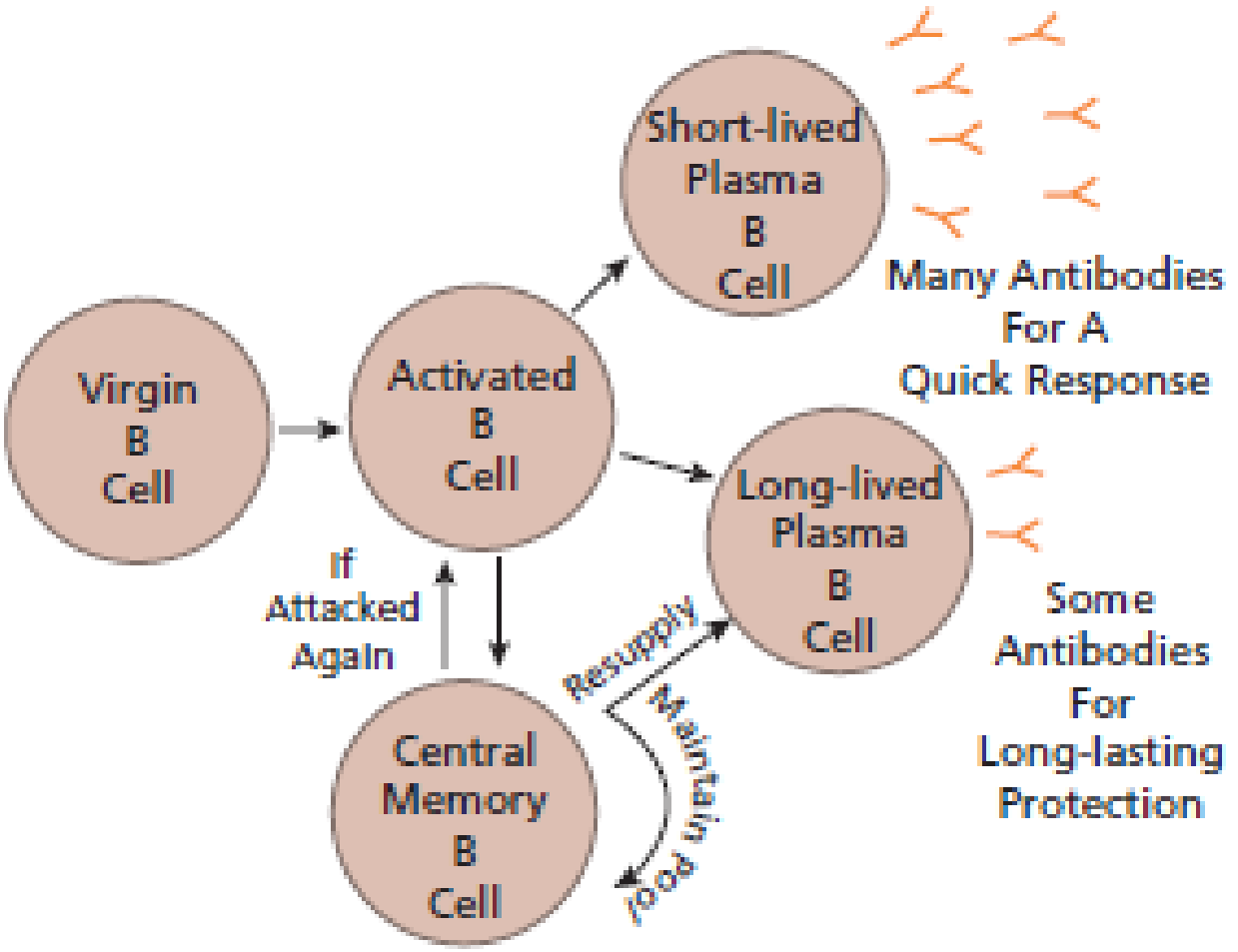
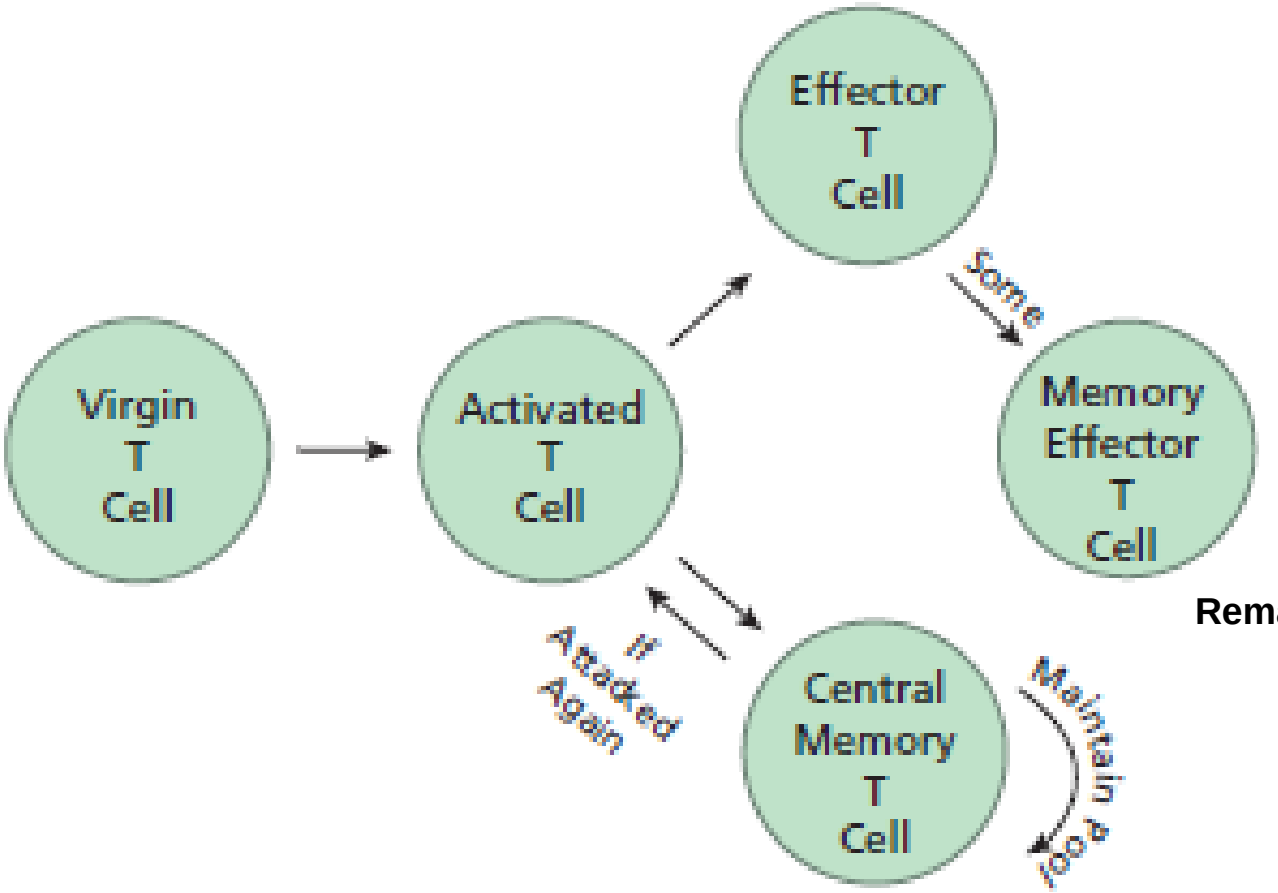

Immunological Memory
Innate Memory
ex: TLRs, Ancestor pathogens
Not updatable in our lifetime
Adaptive Memory
(B cell and T cell memories)
Lifetime pathogens
Updatable and unique for every individual

B cell memory



2°lymphoid organs

T cell Memory



Properties of Memory Cells

1- More numerous in the circulation than naive ones (1000X more).

2- Memory B and T cells are easier to activate:
(Less dependent on co-stimulation)

3- Memory B cells are already class-switched.

4-Memory B cells produce antibodies that have undergone somatic hypermutation.

Comparing B and T cell memories

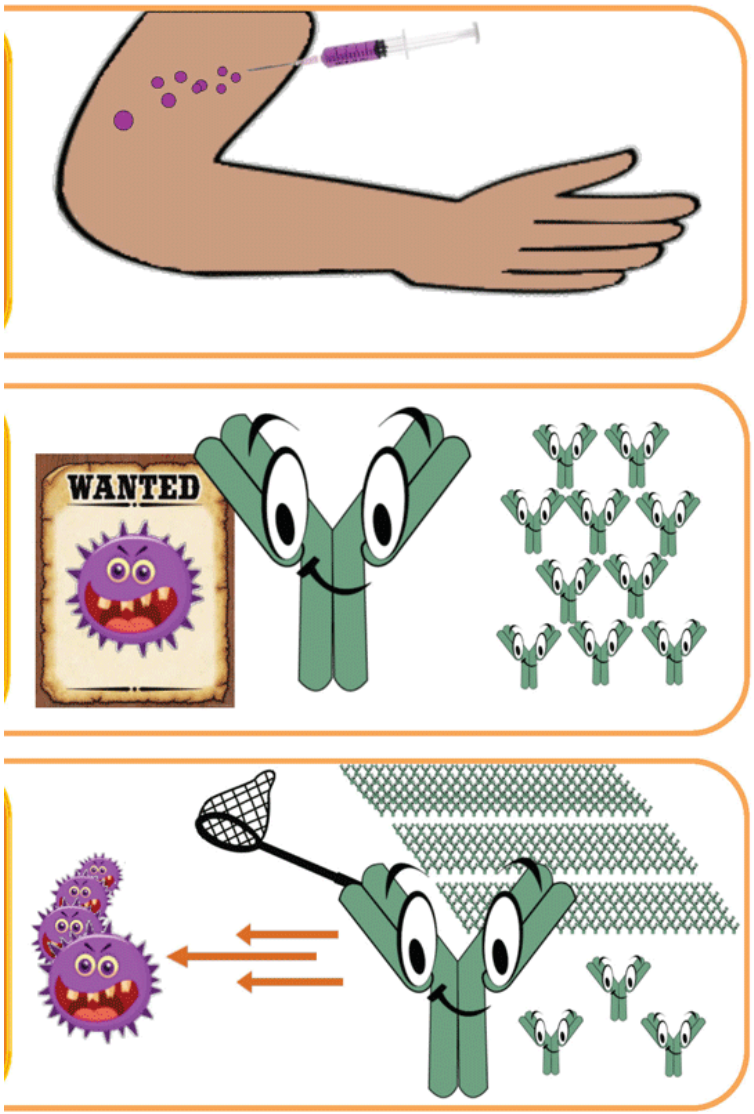
	B Memory	**T Memory**
Stem-cell-like cell memory	Yes	Yes
Somatic Hypermutation	Yes	No
Remain active after infection is done?	**Yes**, produce abs for life.	**No**, effector T cells go dormant

Maintenance of B and T cell memory

Remnants of the pathogen in secondary lymphoid tissue (Restimulation)

Cytokine and ligand-mediated slow proliferation of T and B memory cells without the presence of any pathogen remnant.

Vaccines



We are not only talking about antibodies but also about memory helper T and B cells

When do we produce memory killer T cells?

(Attacker infecting APCs or cross-presentation)

Strategies for Vaccine Development

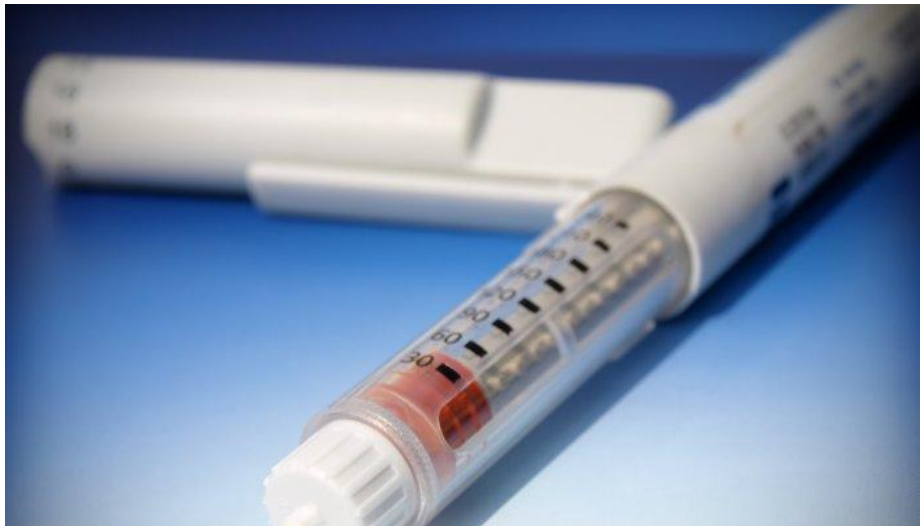
Vaccine should not affect health or lifestyle of patient.

Another challenge in Vaccine development is to find out which memory cell is required for protection.

Ex: Antibodies against HIV are not sufficient for protection.

Usually Memory Killer T cells are required:

This requires APCs to be infected by the virus...Too risky!



Non-infectious Vaccines

Examples: Salk Vaccine for **Polio**, **Flu** vaccine, **Typhoid** and **Pertussis** vaccines.

-Whole organism inactivated by a chemical, ex: Formaldehyde (risky)

-Toxoids made of toxins (**Diptheria**, **tetanus**)
-Certain parts of pathogens: Acellular **pertussis** vaccine.
-Genetically engineered viral proteins: **Hep B** and **HPV** vaccine

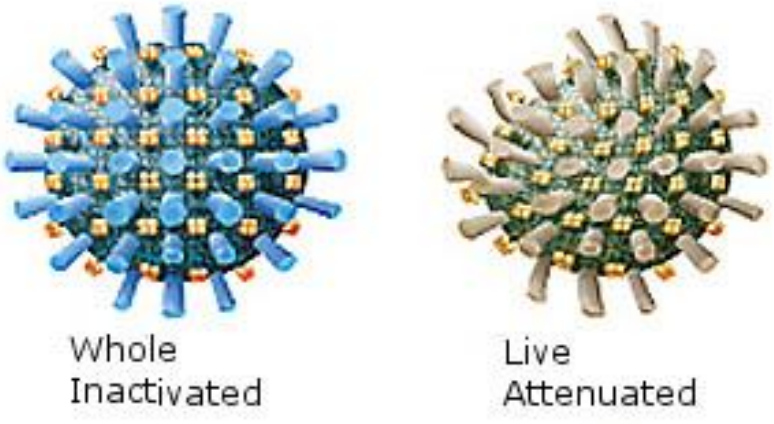
Drawbacks: Will not generate memory Killer T cells

Attenuated Vaccines

Ex: Vaccine for Measles, Mumps, and Rubella (MMR), Sabin Polio virus (grown in monkey kidney cells instead of human nerve cells).

Advantages: Produce memory Killer T cells

Drawbacks: Vaccine can infect people with a weak immune system,
Vaccine can mutate back to wildtype in rare cases.



Carrier Vaccines

Introducing a single (or few) genes of the pathogen into a virus that doesn't cause disease.

Advantages: Can induce memory killer T cells
Safe

This method was tried in Thailand with an HIV vaccine; modest results!

Will there be an AIDS vaccine?

Effective Vaccine must generate memory Killer T cells.

Non-infectious approach- Cannot work → No memory Killer T cells produced

Attenuated approach → Could generate memory Killer T cells, but too risky due to virus high mutation rate.

Carrier Vaccine → Could generate memory Killer T cells, but so far modest results ex: Thailand study.

Even if memory CTL is produced, it will not be effective against mutated viruses!

High mutation rate is a huge challenge in Vaccine development.

Work is being done on discovering broadly neutralizing HIV antibdoies.

HIV is not the only obstacle: Malaria, *Leishmania*, tuberculosis, HSV. (no vaccine!)

?Any question