# Kuby Immunology (Chapter 1)

## ① Cell Mediated Immunity

→ proposed by Metchnikoff.
→ lymphocyte → identified as responsible for both cell-mediated and humoral immunity

⇒ Cellular immunity — T cells } →
Humoral immunity — B cells }

→ Defining an antigen — anything that elicits a specific response by B or T lymphocytes

→ Landsteiner demonstrated unparalleled levels of recognition for diverse antigens — size of lymphocyte repertoire is about $10^9$.

→ gave rise to the selective and the instructional theory
↳ proved correct

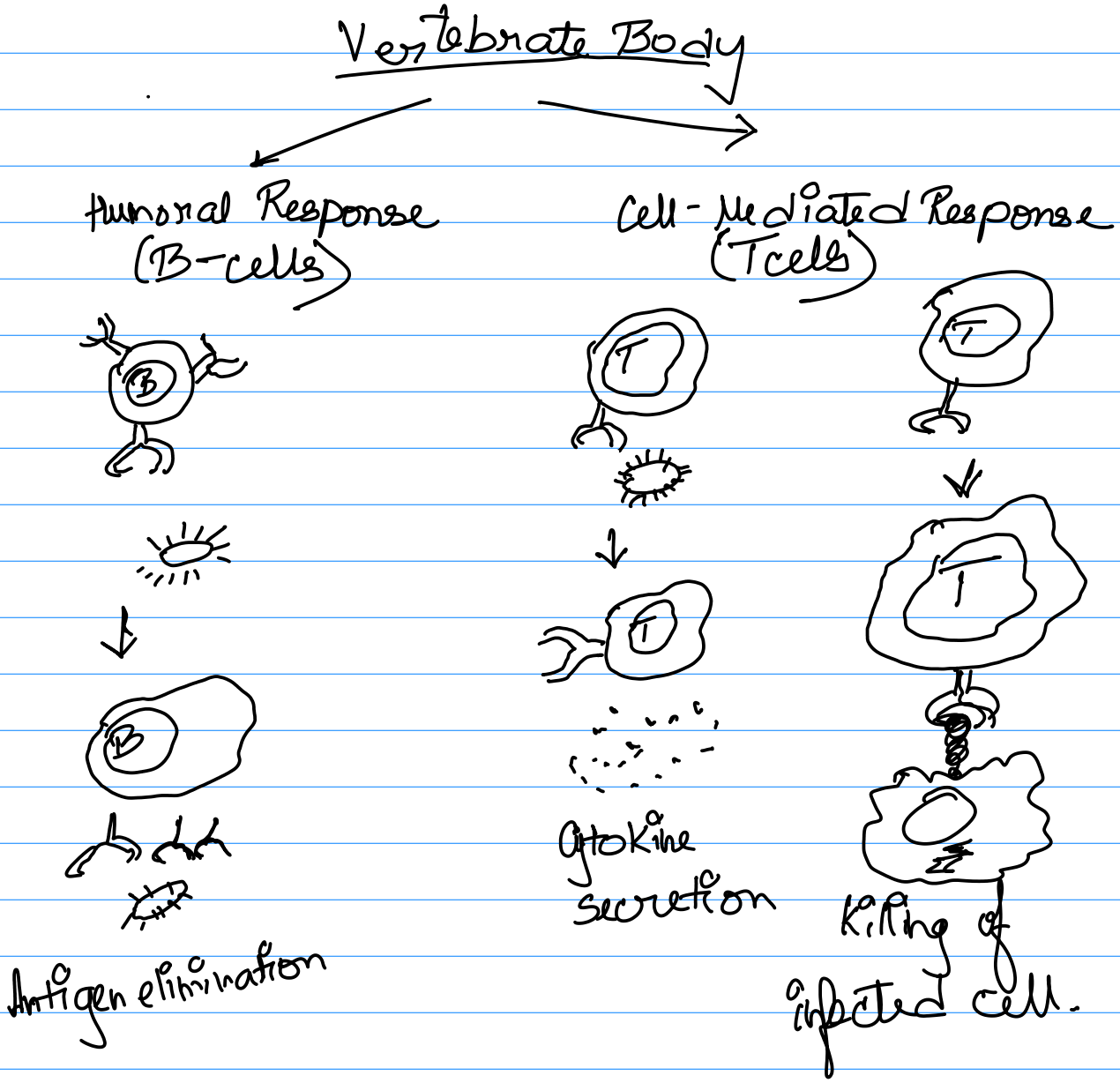
Selective theory:

① Cells have specific receptors even before exposure to antigens.

② Each cell expresses membrane bound receptors of just one specificity, called antibodies in their soluble form.

developed into the clonal selection theories:

- Individual B or T lymphocyte - expresses many copies of a membrane receptor that is specific for a single distinct antigen.
- Binding of antigen to the receptor activates the cell, causing it to proliferate into a clone of daughter cells that have the same receptor specificity as the parent cell.



Organisms causing disease → Pathogens

- viruses
- fungi
- parasites
- bacterias.

Effective defense lies in terms of invading pathogen.

(whether it resides inside or on surface of host cells.

Pathogen recognition needs interaction between antigenic fragment and recognition molecule.

Immune response — intracellular or extracellular cascade of events that leads to labelling and destruction of pathogen.

What happens for viruses?

Viruses live in the cell — as obligate parasites ⟹ something is needed to recognise changes in host cells once they are infected — done by cytotoxic T cells

## PAMPs

→ Pathogen associated molecular patterns
→ part of innate immunity & consists of common structures that recognise whole groups of pathogens.

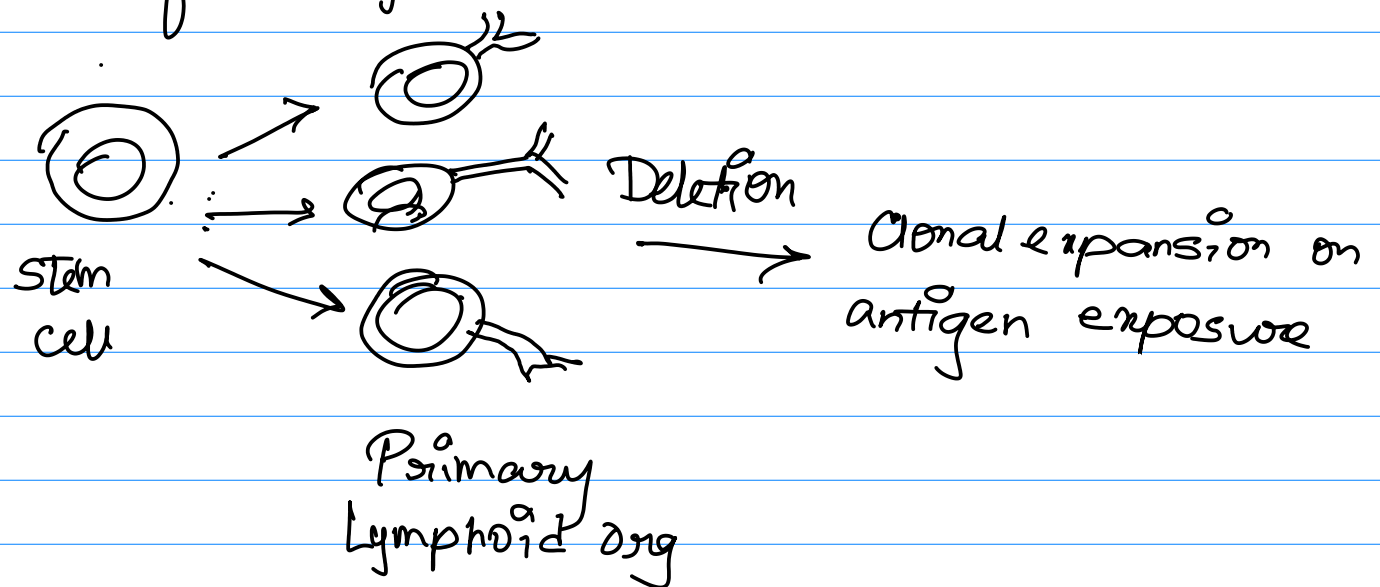
→ Pattern Recognition Receptors (PRRs) specifically recognise PAMPs and label antigen for destruction

→ Conserved and germline encoded recognition molecules.

## Generation of Diversity

- Diversity of pathogen antigenic site changes randomly through mutation.
In order to keep up — ongoing arms race with host immune system.

Sol$^n$ Randomness is favoured in the generation of recognition molecules.



## Generation of diversity

↳ Germline Theory – Permutation combination of different light and heavy chain antibodies.

↳ Minigene Hypothesis

– basically VD(J) recombination.

↳ Somatic hypermutation – High rate of point mutation of the variable and D & joining regions of HC & LC.

## Tolerance

Hallmark – immune system must not attack host tissues

↳ system of checks — to establish Tolerance

unresponsiveness against host structures

## Central Tolerance

process by which newly developed B and T cells are rendered non-reactive to self.

# Clonal Selection

positive selection
(maturation of T cells which bind weakly to self MHCs)

negative Selection
(elimination of T cells who express strong binding ability to self antigens present in lymphoid organs.)

Negative selection is important for maintaining central tolerance — expressed a short time after expressing antigen receptors.

↳ those that are reactive to self antigens are efficiently removed by apoptosis

However, not always true. Immature B cells can edit the receptor and thus change the specificity.

Theories that speak of tolerance;

1. Clonal deletion theory — self-reactive lymphocytes are eliminated.
2. Clonal Anergy theory — self-reactive lymphocytes are inactivated.
3. Idiotype Network theory — Natural antibodies neutralising self-reactive antibodies

④ Clonal Ignorance Theory – Self-reactive T-cells migrate to periphery, where autoreact B cells cannot make contact with them.

⑤ Regulatory Tcell: Regulatory T cells preventing or inactivating self-activated responses.

Immunity

Innate Immunity

- PRRS
- complement

Adaptive Immunity

- selection and proliferation of T and B lymphocytes after antigen exposure.

How do they communicate?

→ Achieved by cell-cell contact
→ soluble proteins like cytokines and chemokines.
They recruit new cells to the site, instruct differentiation and release of new protein factors.

## Memory

→ important feature of adaptive immunity
→ secondary response much faster and stronger than primary response. Why?

Because during primary response, the cells with the most efficient affinity are clonally selected and honed.

↳ Further exposure → memory cells → kin of the final and most efficient trained cells are re-recruited.

Flowchart of immune response:

Bacteria breach physical barrier

↓

Phagocytosis

↓

Phagocyte releases cytokines and chemokines to attract other WBCs.

↓

Phagocyte travels to local lymph node → carries bacterial antigens to B- and T cells

↓

Adaptive immune response through activation

↓

Activated $T_H$ cells activate B cells and clonal expansion of both happen at lymph node

↓

Immune Response & Memory Cell Creation.