Immune Regulation

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Objectives

- What is immune regulation?
- Why we need it?
- What are the mechanisms of immune regulation?
- What is central tolerance?
- What is peripheral tolerance?

Why is immune regulation important?

- If not regulated properly, it can cause harm to host

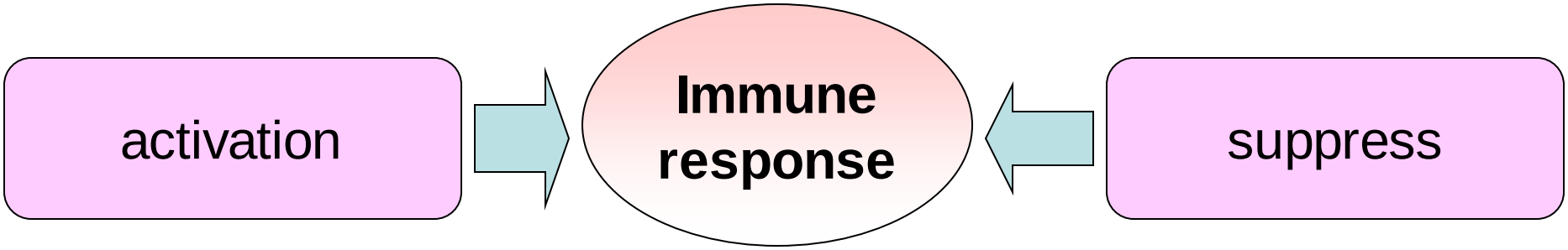
- If defective--------> Immunedeficiency ----> severe infections
  cancers
- If exaggerated------> Hypersensitivity
  tissue destruction
- If inappropriate -------> Autoimmunity -----> immune response to self tissues

Immune Regulation

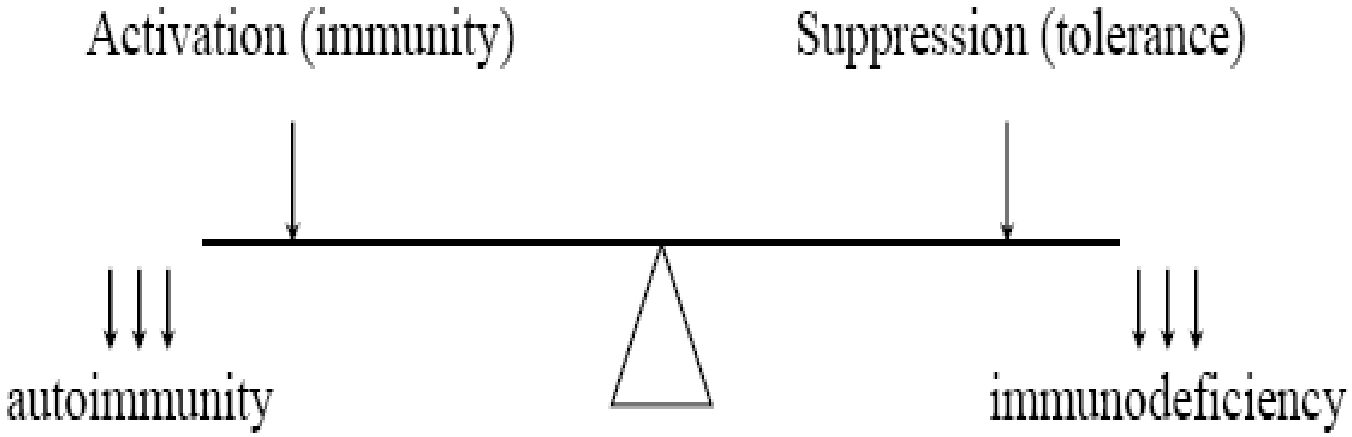
- A balance between
  - activation and
  - suppression

  } of effector cells

- to achieve an efficient immune response without damaging the host.



Immune Regulation



- Natural regulatory mechanisms
- Artificial regulatory mechanisms

Natural Regulatory Mechanisms

Immune Regulation

- Regulatory mechanisms act at all phases of immune response
  - Recognition
  - Activation
  - Effector function

Immune Regulation

- The immune system should react against foreign antigens, but not self antigens
- The activated immune system should be turned off when the foreign antigen is killed
- The immune system should be unresponsive to self antigens

“ immunological tolerance”

Tolerance
Burnet's Hypothesis:(1949)

- During neonatal stage of life, or when immune system is developing, all Ags present are recognized as self.

- Immune system becomes tolerant to these Ags

How does immune system discriminate “self” from “non-self”?

1. Innate immune system
2. Adaptive immune system

Mechanisms of Innate immune system

- Cells of innate immune system has receptors (Pattern recognition receptors) to identify broadly expressed molecules shared by broad groups of microbes ("pathogen-associated molecular patterns" PAMPs) e.g. – bac DNA, LPS, teichoic acid
- They are only present on microbes not on self tissues

- Mechanisms of unresponsiveness to self tissues by
  1. Ignorance (lack of recognition) of self cells (unless they change their surface structures)
  2. Presence of inhibitory structures/ receptors

Mechanisms of Adaptive system

- Lymphocytes with receptors capable of recognizing self antigens are constantly being generated in adaptive system

- Immune system is readily accessible to self antigens

? Big problem

How these self reactive lymphocytes are eliminated?

1)Central tolerance – is induced by "Negative selection"

- T cells in thymus
- B cells in bone marrow

} cells die by "Apoptosis"

2) Peripheral tolerance – is induced by Anergy or Apoptosis

T cells - Ag recognition without costimulation (2nd signal)

B cells - Ag recognition without T cell help or blocking of signaling pw - "partial activation"

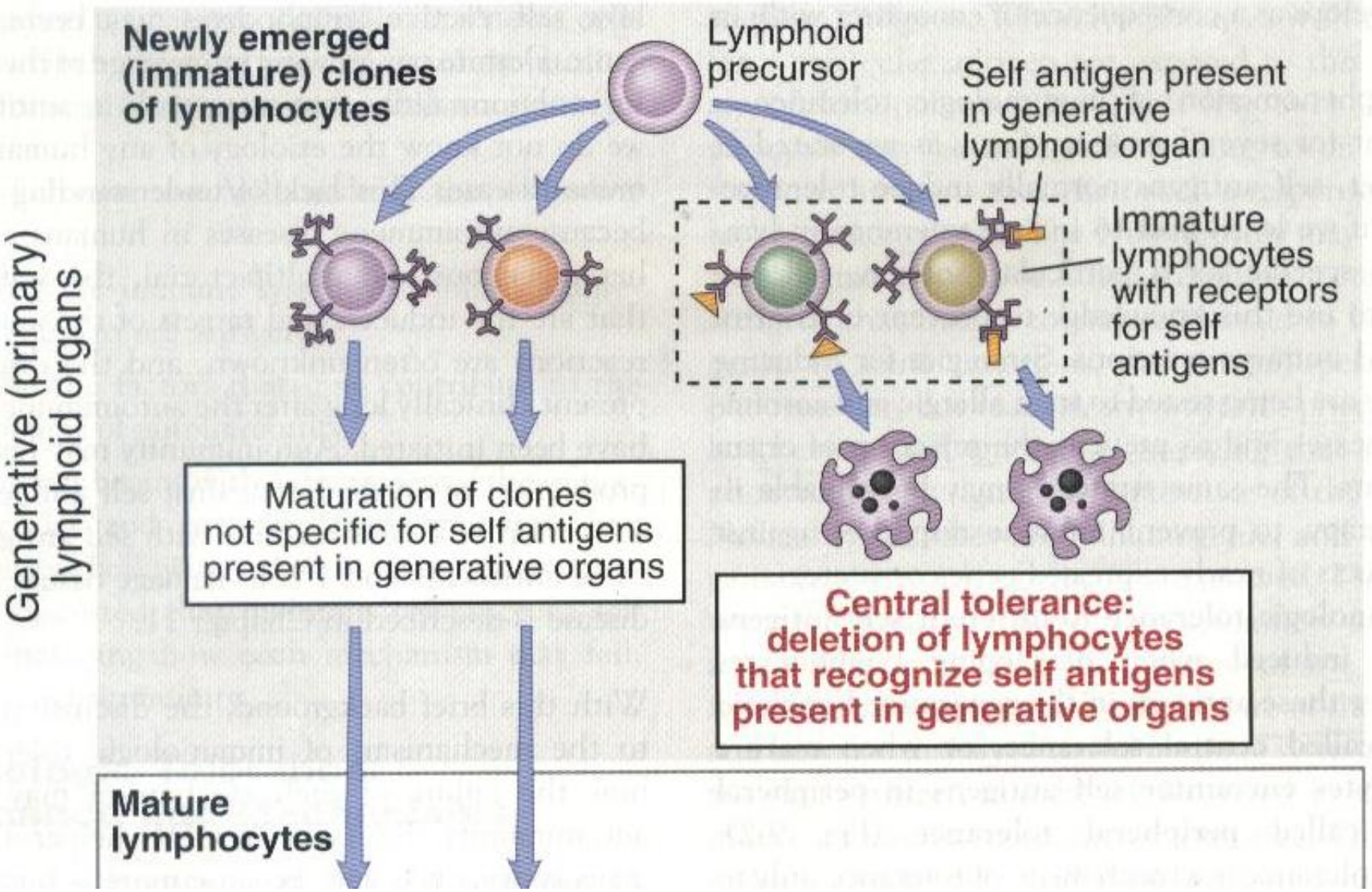
3) Regulatory T cells

What is central tolerance?

- Process whereby immature T and B cells acquire tolerance to self antigens during maturation in primary lymphoid organs.

- If an immature lymphocyte strongly recognizes and interacts with a self antigen (present in bone marrow and thymus) ---------> dies by a process called apoptosis before it can complete its maturation ---**clonal deletion**

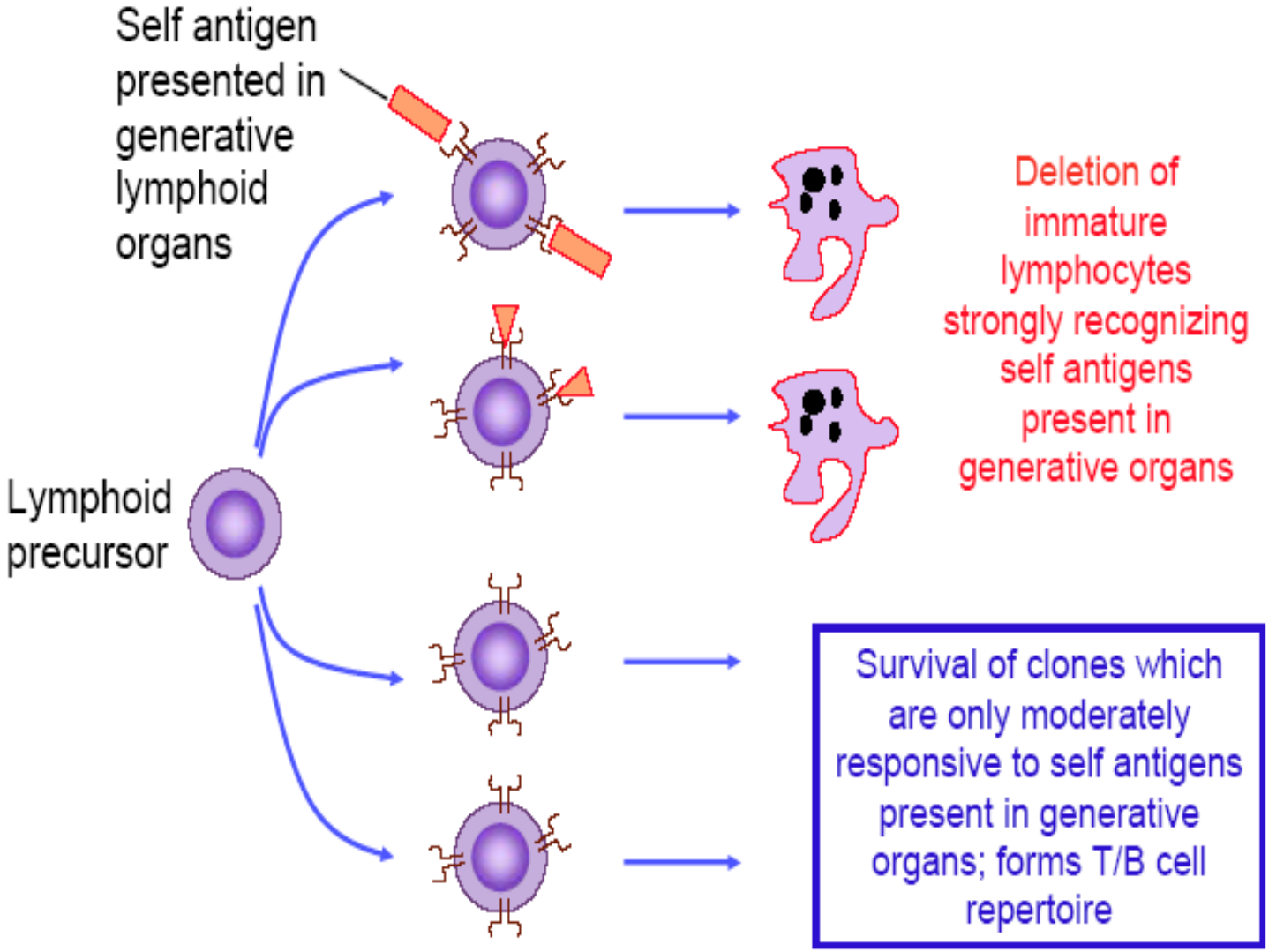
"Negative selection"



lymphocytes that survive negative selection move to peripheral lymphoid organs

Mechanisms of unresponsiveness:

Central tolerance in B and T cells (I): Clonal Deletion



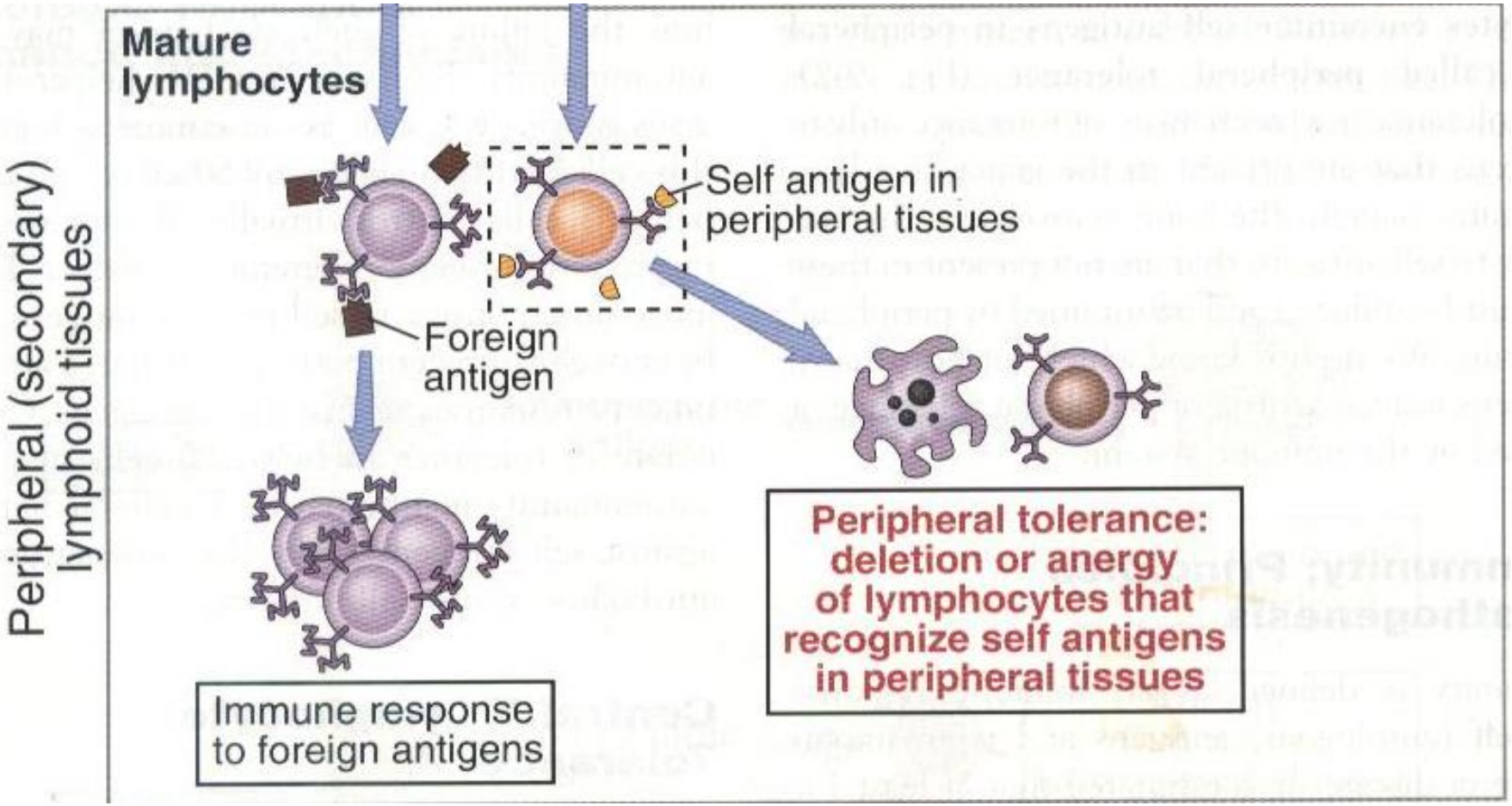
Negative selection

Positive selection

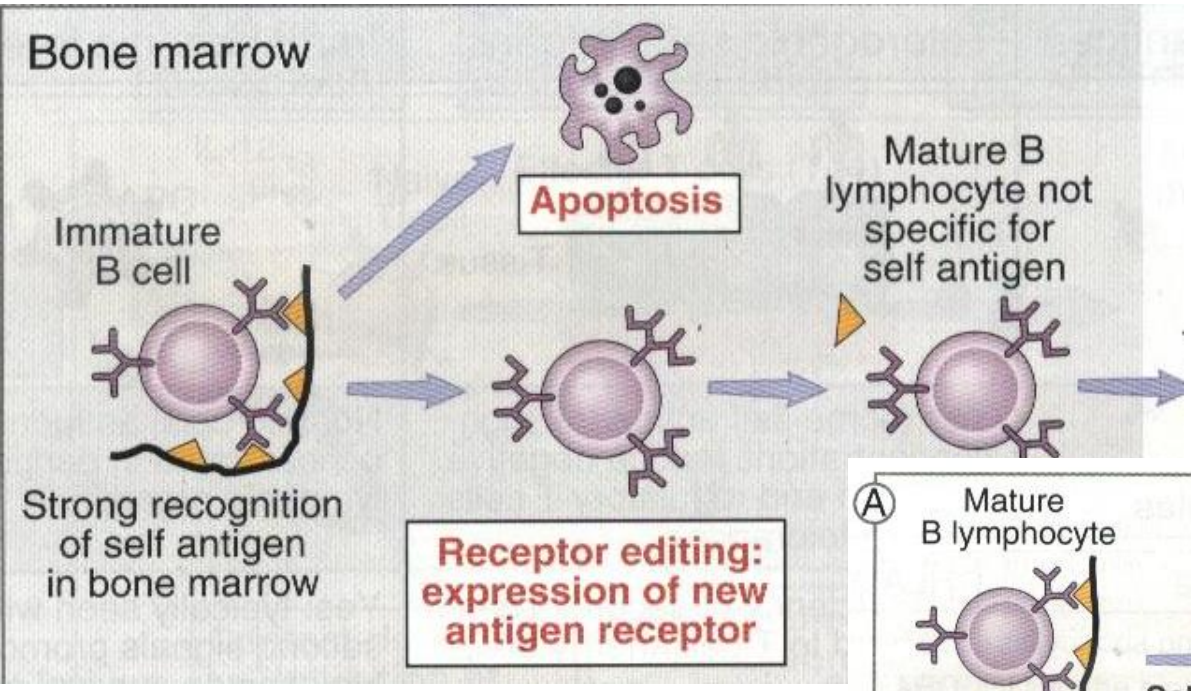
What is peripheral tolerance?

- Process whereby mature T and B cells acquire tolerance to self antigens present in secondary lymphoid organs

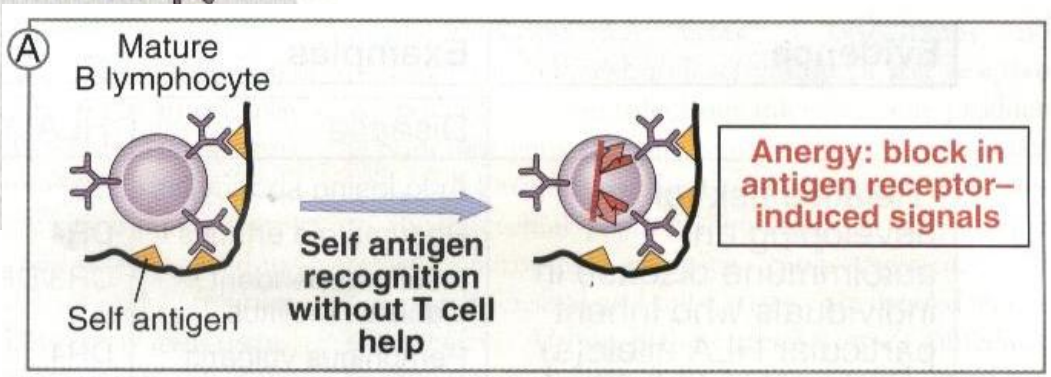
- When mature lymphocytes recognize antigens without 2nd signal needed for their full activation
  - Anergy (alive but functionally hyporesponsive/ inactivated)
  - Apoptosis (programmed cell death)

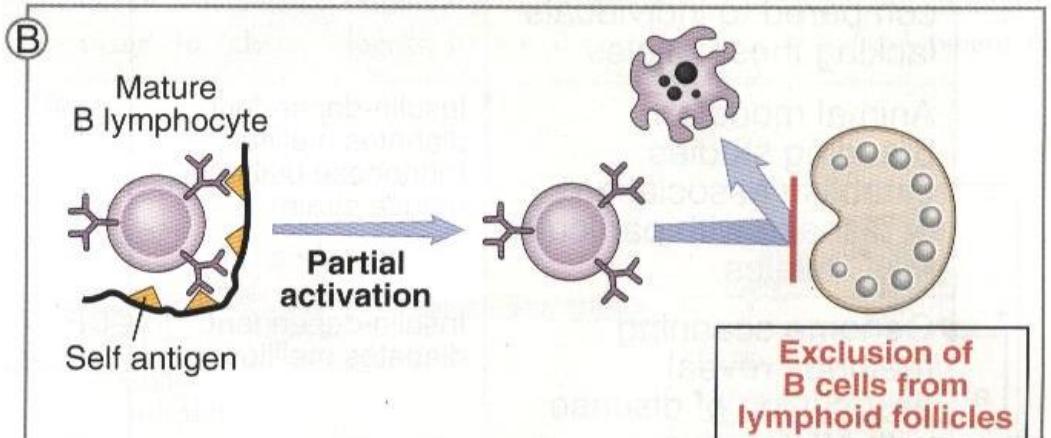

Peripheral (secondary) lymphoid tissues
Mature lymphocytes
Self antigen in peripheral tissues
Foreign antigen
Immune response to foreign antigens
Peripheral tolerance: deletion or anergy of lymphocytes that recognize self antigens in peripheral tissues

B cell tolerance



peripheral LO





What are the 2 signals required for T cell activation?

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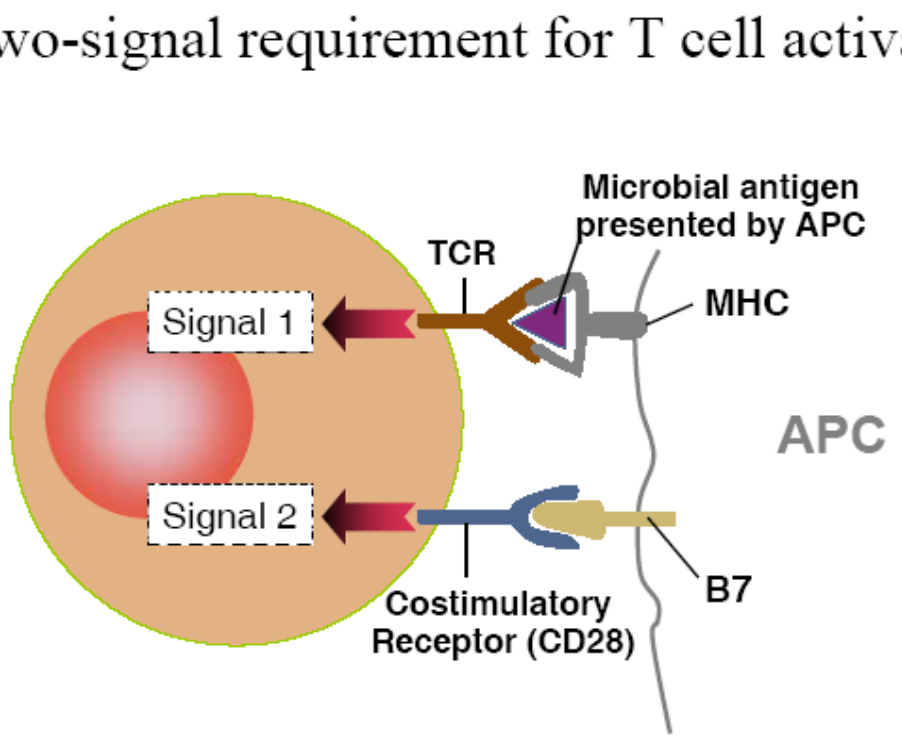

Regulatory T cells

- Some immature T cells that recognize self antigens in thymus develop into regulatory T cells

- They enter peripheral tissues and produce cytokines that block the activation of self reactive lymphocytes

Consequences of encounter of lymphocytes with Ags

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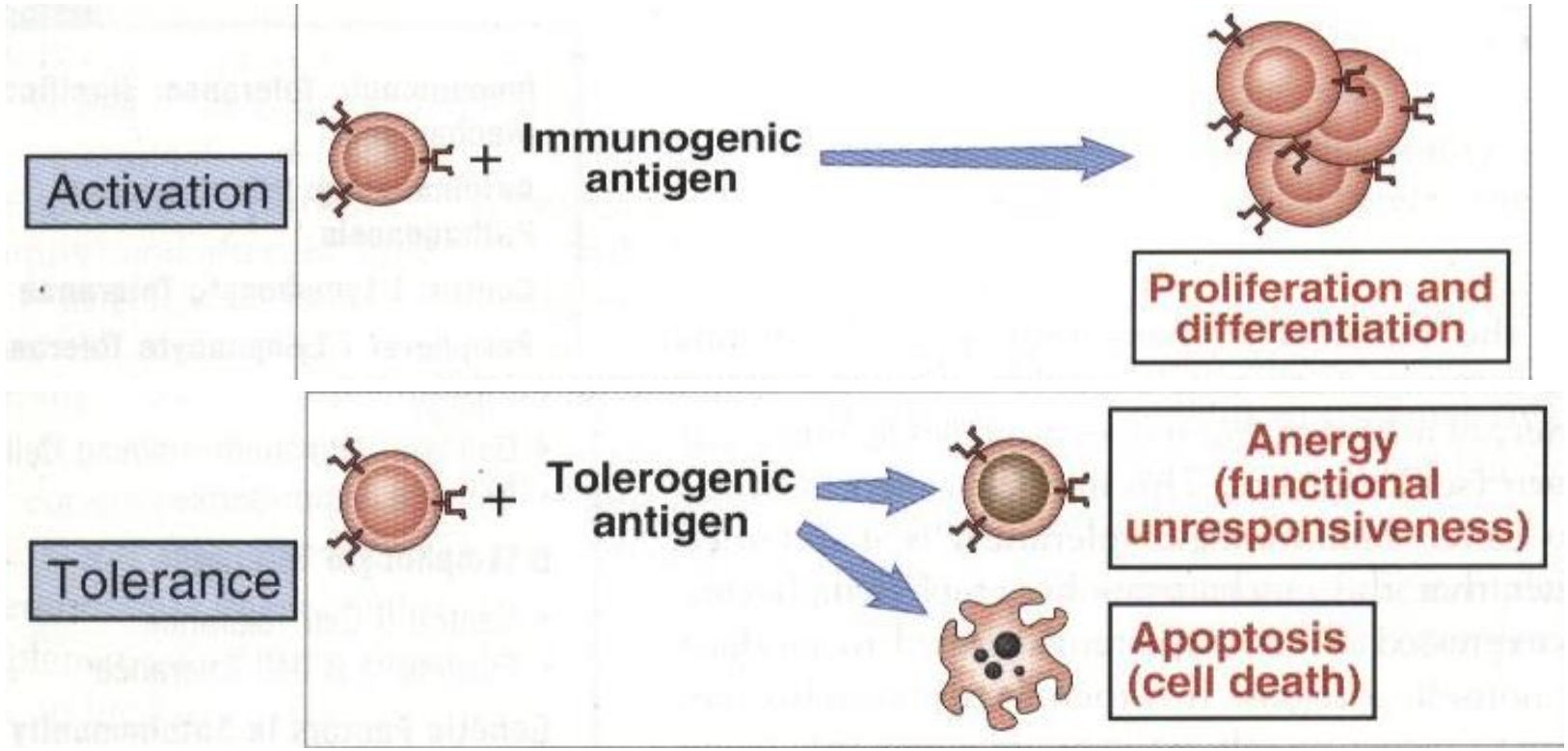

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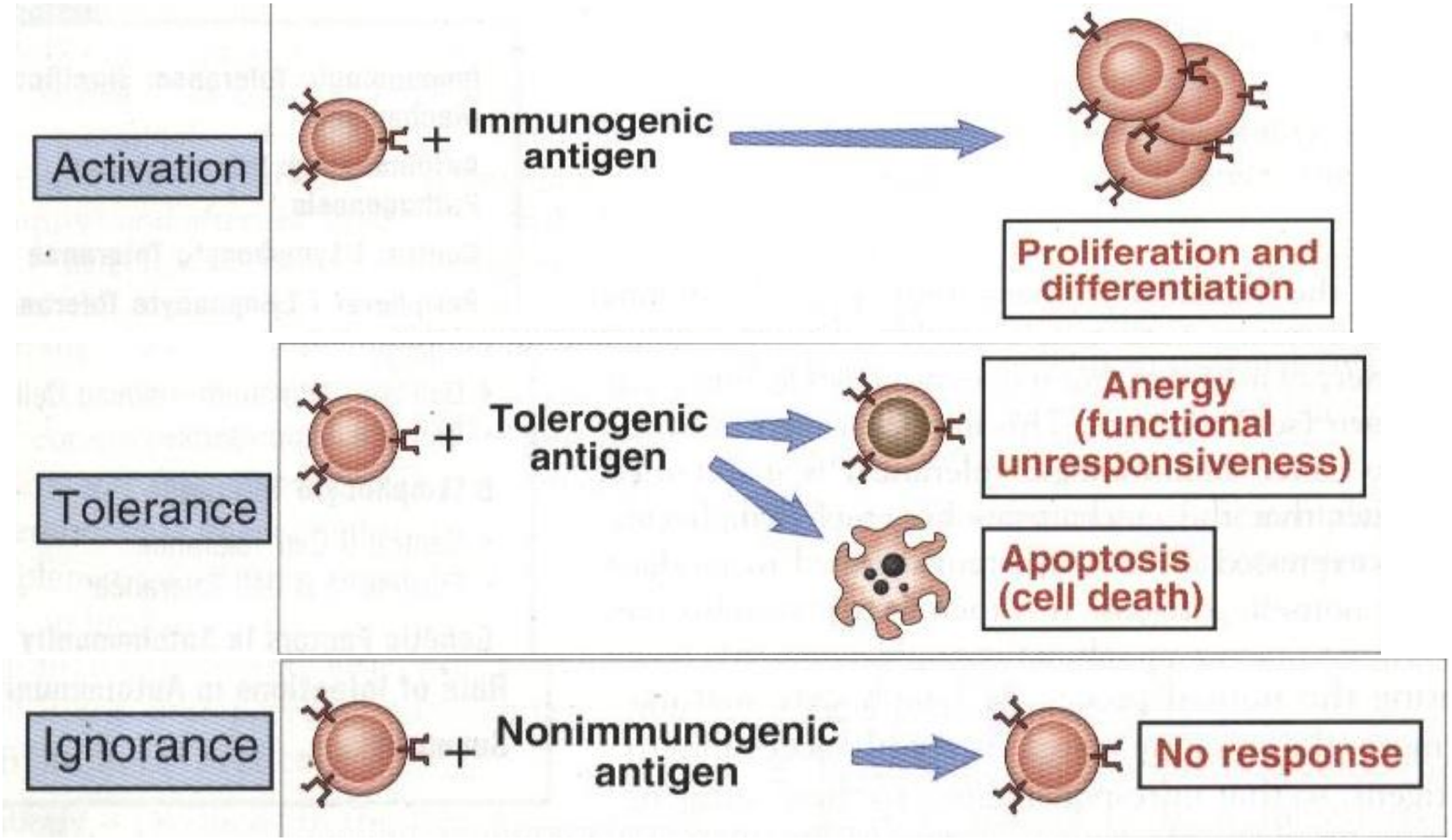

Artificial Regulatory Mechanisms

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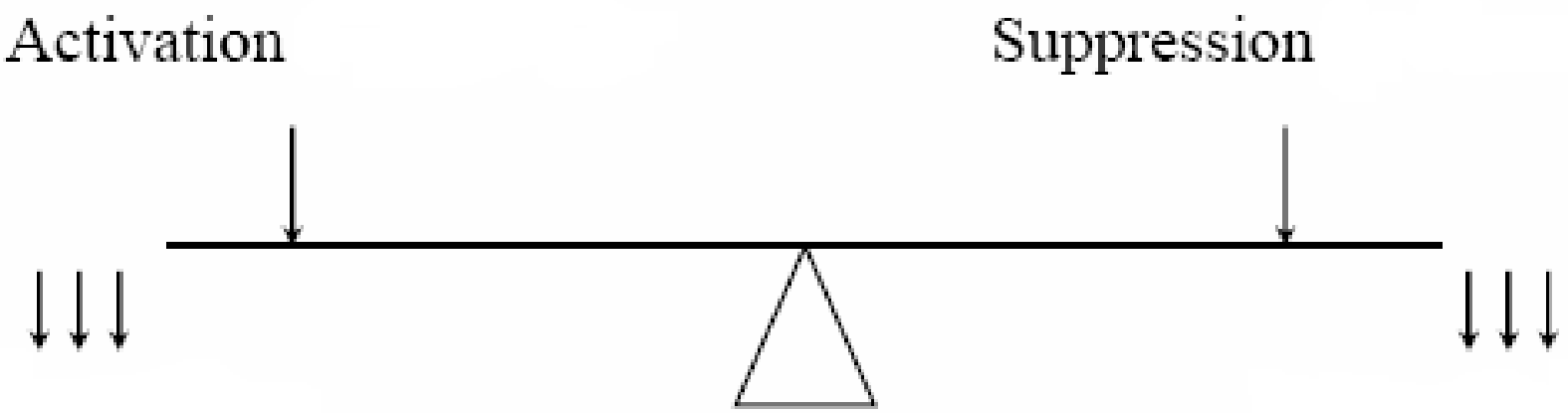


Immuno-potentiaition

Immuno-suppression

Given For –

Prevention of infection

Treatment for infection/ca

Patients with immune deficiency

Given For –

Prevention of graft rejection

Treatment of Autoimmunity

Immune-modulation

- Can be done artificially to

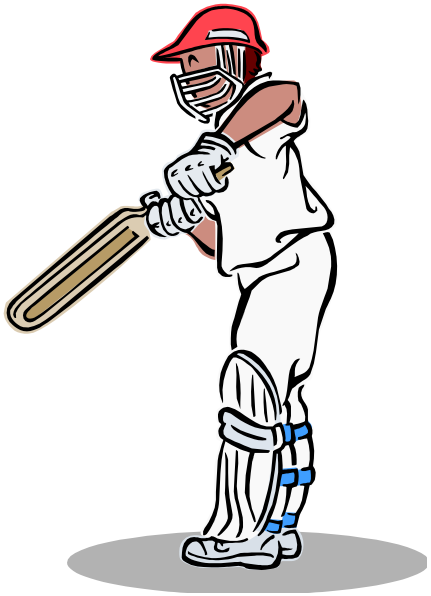
  -->Potentiate / stimulate immune response

  -->Suppress immune response

E.g.

Potentiate - by giving Vaccines, antibodies, effector T cells, cytokines, adjuvants

Suppression – by immuno-suppressive drugs, ionizing radiation



Any Questions?


Thank You