

## Immunological tolerance

- Immunological tolerance is a state of unresponsiveness to an antigen induced by the exposure of specific lymphocytes to that antigen, but respond to other antigens normally.
- Like immunological memory, immunological tolerance is antigen specific. It can exist in B cells, T cells or both
- **Self-tolerance:** Normal individuals are tolerant of their own antigens (self-antigen). Immunological tolerance is classified into: -central tolerance or peripheral tolerance depending on where the state is originally induced- either in the thymus and bone marrow (central) or in other tissues (as spleen) and lymph nodes (peripheral).

## Central tolerance

- Central tolerance refers to the tolerance established by deleting auto-reactive lymphocyte clones before they develop into fully immune-competent cells. It occurs during lymphocyte development in the thymus and bone marrow for T and B lymphocytes, respectively.
- In these tissues, maturing lymphocytes are exposed to self-antigens presented by medullary thymic epithelial cells and thymic dendritic cells, or bone marrow cells. Those lymphocytes that have receptors that bind strongly to self-antigens are removed by induction of apoptosis (programmed cell death) of the autoreactive cells, or by induction of energy, a state of non-activity. **Peripheral tolerance**
- Peripheral tolerance develops after T and B cells mature and enter the peripheral tissues and lymph nodes.
- Inappropriate reactivity toward normal, self-antigen that was not eliminated in the thymus can occur, since the T cells that leave the thymus are relatively but not completely safe. Some will have receptors (TCRs) that can respond to tissue specific self-antigens.

**Peripheral tolerance:** Those self-reactive T cells that escape intra-thymic negative selection in the thymus can inflict cell injury unless they are deleted or effectively inactivated in the peripheral tissue chiefly by natural regulatory T cells (nTreg cells)

### **Physiological importance of immunological tolerance**

- Immunological tolerance is the main way the immune system learns to discriminate self from non-self, thus preventing autoimmunity.
- Peripheral tolerance is key to preventing over reactivity of the immune system to various environmental entities (allergens, gut microbes, etc.)
- Immune tolerance in pregnancy is what allows a mother to gestate a genetically distinct offspring with an immune response (a response to non-self-antigens from members of same species) muted enough to prevent miscarriage.

### **Applications of immunological tolerance**

In medicine Immunological tolerance can be induced artificially that may eventually be exploited clinically to:

- Prevent rejection of transplanted organs
  - Treat autoimmune diseases
  - Treat allergic diseases
- Negative impacts of immunological tolerance on health
- It allows some pathogenic microbes to successfully infect a host and avoid elimination.
  - In addition, inducing peripheral tolerance in the local microenvironment is a common survival strategy for a number of tumors.