

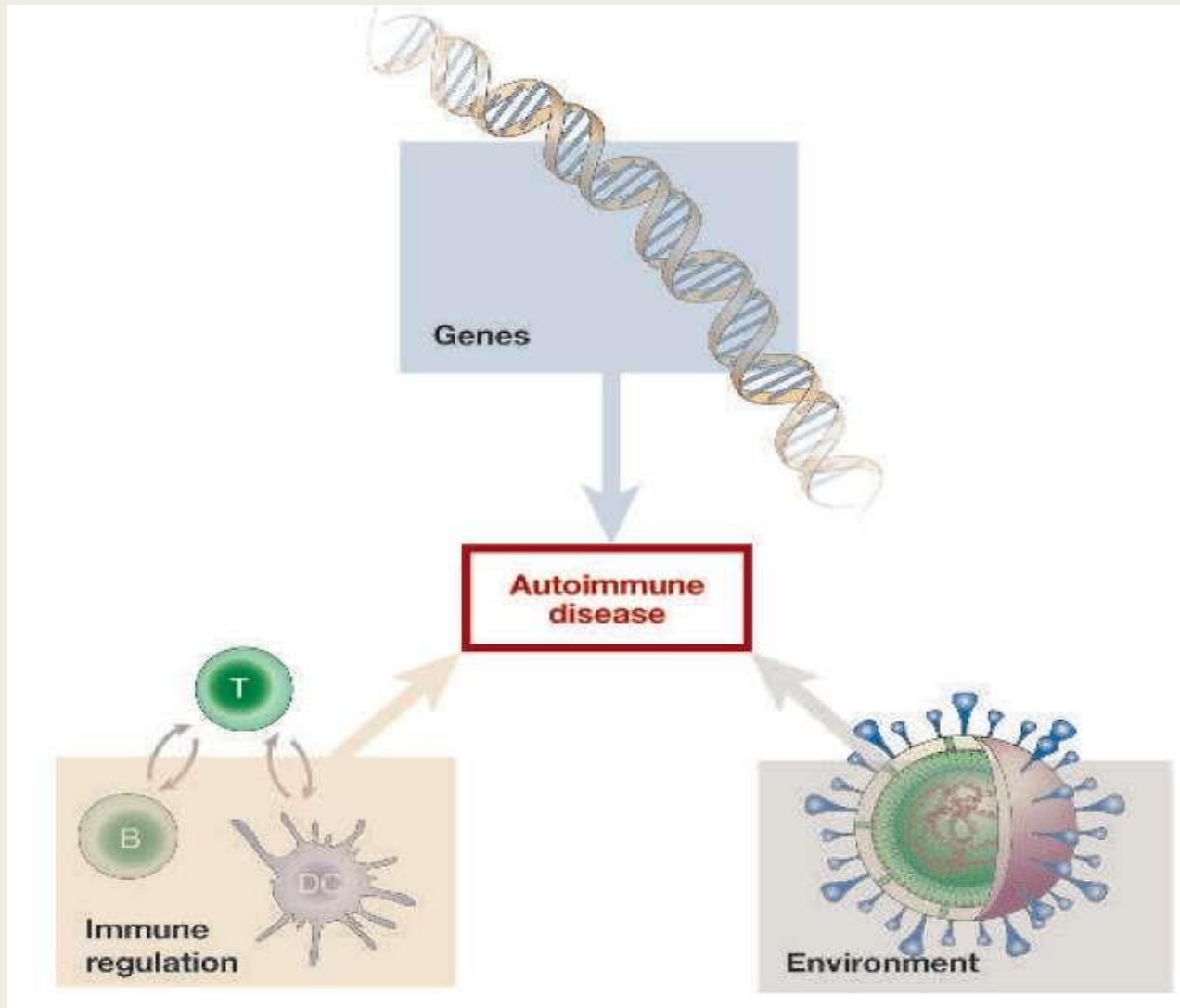
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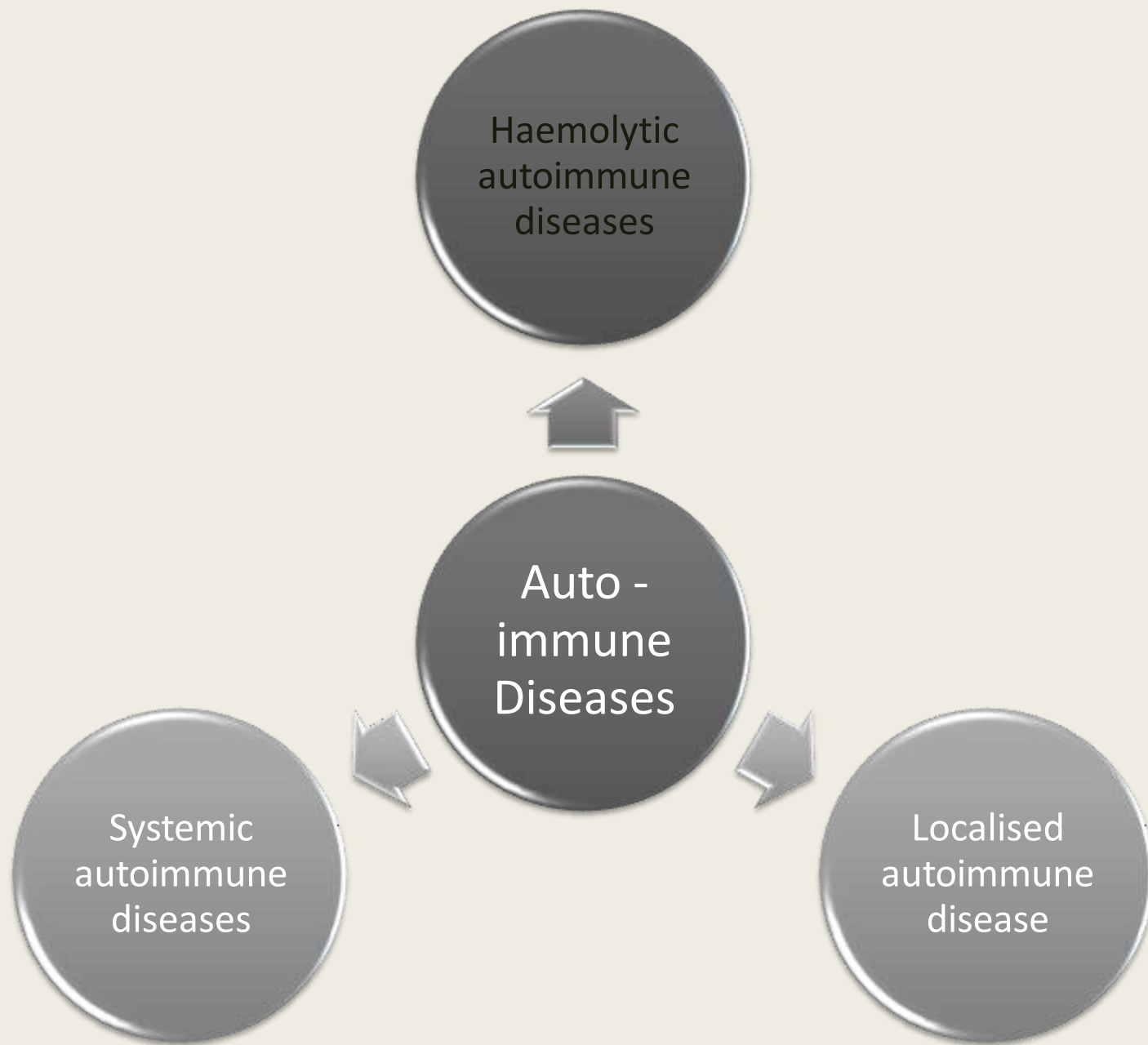
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Introduction

- Autoimmune diseases is a group of disorders in which tissue injury is caused by humoral (by auto-antibodies) or cell mediated immune response (by auto-reactive T cells) to self antigens.
- An autoimmune disorder may result in:
 - The **destruction** of one or more types of body tissue
 - **Abnormal growth** of an organ
 - **Changes** in organ function

Causes of Autoimmunity





1. Haemolytic autoimmune diseases

- Clinical disorder due to destructions of blood components. Auto Ab are formed against one's own RBCs, Platelets or Leucocytes .
- E.g. Haemolytic anaemia, Leucopenia, Thrombocytopenia, etc.

2. Localised autoimmune disease

- A particular organ is affected due to autoAbs.
- For example:
 - **Thyroiditis** (attacks the thyroid)
 - **Multiple sclerosis** (attacks myelin coating of nerve axons)
 - **Myasthenia gravis** (attacks nerve-muscle junction)
 - **Juvenile diabetes** or Type I DM (attacks insulin-producing cells)

Hashimoto's thyroiditis

- Hypothyroidism & destruction of thyroid cells.
- Characterised by Goitre, enlarged thyroid gland.
- Characterized by Type IV hypersensitive reactions.
- It is a T-cell associated auto immune disease .

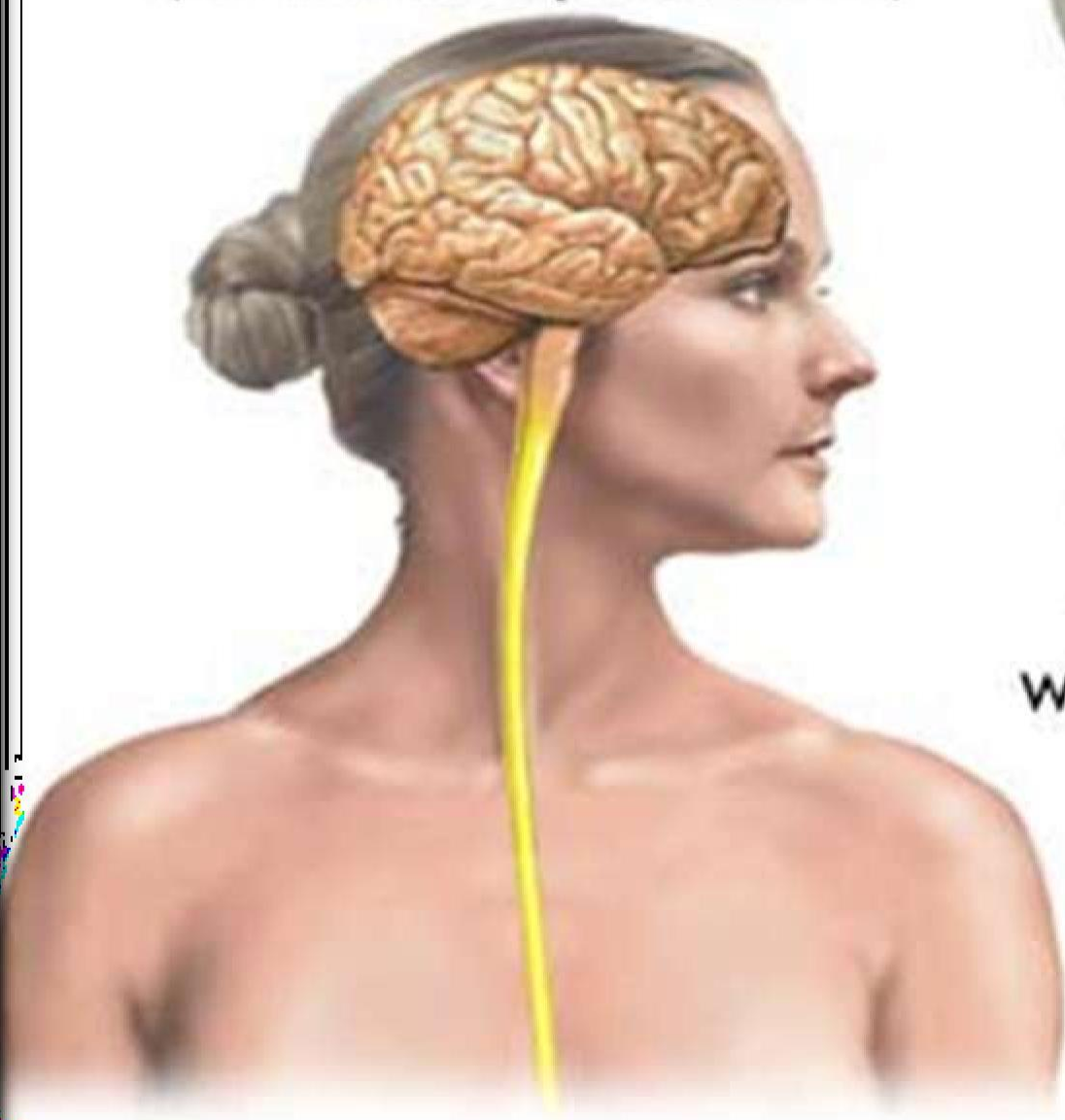
Myasthenia Gravis

- Caused by auto antibody against muscle
- Antigen & acetylcholine receptor antigen.
- Characterized by ↑muscular weakness
- Eventually death from respiratory failure .
- Neuromuscular junction is severely affected.

Multiple Sclerosis

- Degeneration of nerves CNS (brain and spinal cord).
- Myelin disappear due inflammation.

Central nervous system (brain and spinal cord)



In multiple sclerosis the myelin sheath, which is a single cell whose membrane wraps around the axon, is destroyed with inflammation and scarring

Type I diabetes

- β cells produce little or no insulin.
- Heritable
- Symptoms are like being very thirsty, hungry, tired or fatigued, urinating more often.

3. Systemic autoimmune disease

- Non organ-specific autoimmune diseases
- Immune complexes accumulate in many tissues and cause inflammation and damage.
- For example:
 - **Systemic Lupus Erythematosus** (anti-nuclear Ab.): Harms kidneys, heart, brain, lungs, skin.
 - **Rheumatoid Arthritis** (anti-IgG antibodies): Joints, hearts, lungs, nervous system.
 - **Rheumatic fever**: cross-reaction between antibodies to streptococcus and auto-antibodies.

Systemic Lupus Erythematosus (SLE)

- Skin disease due to the production of antinuclear factor (ANF) .
- In these patients, **LE cell** (a mature neutrophil) appears in blood & bone marrow
 - Function – Phagocytosis in the presence of ANF.

Most common symptoms of Systemic lupus erythematosus

Systemic:
- Low-grade fever
- Photosensitivity

Psychological
- Fatigue
- Loss of appetite

Mouth and nose
- Ulcers

Face
- Butterfly rash

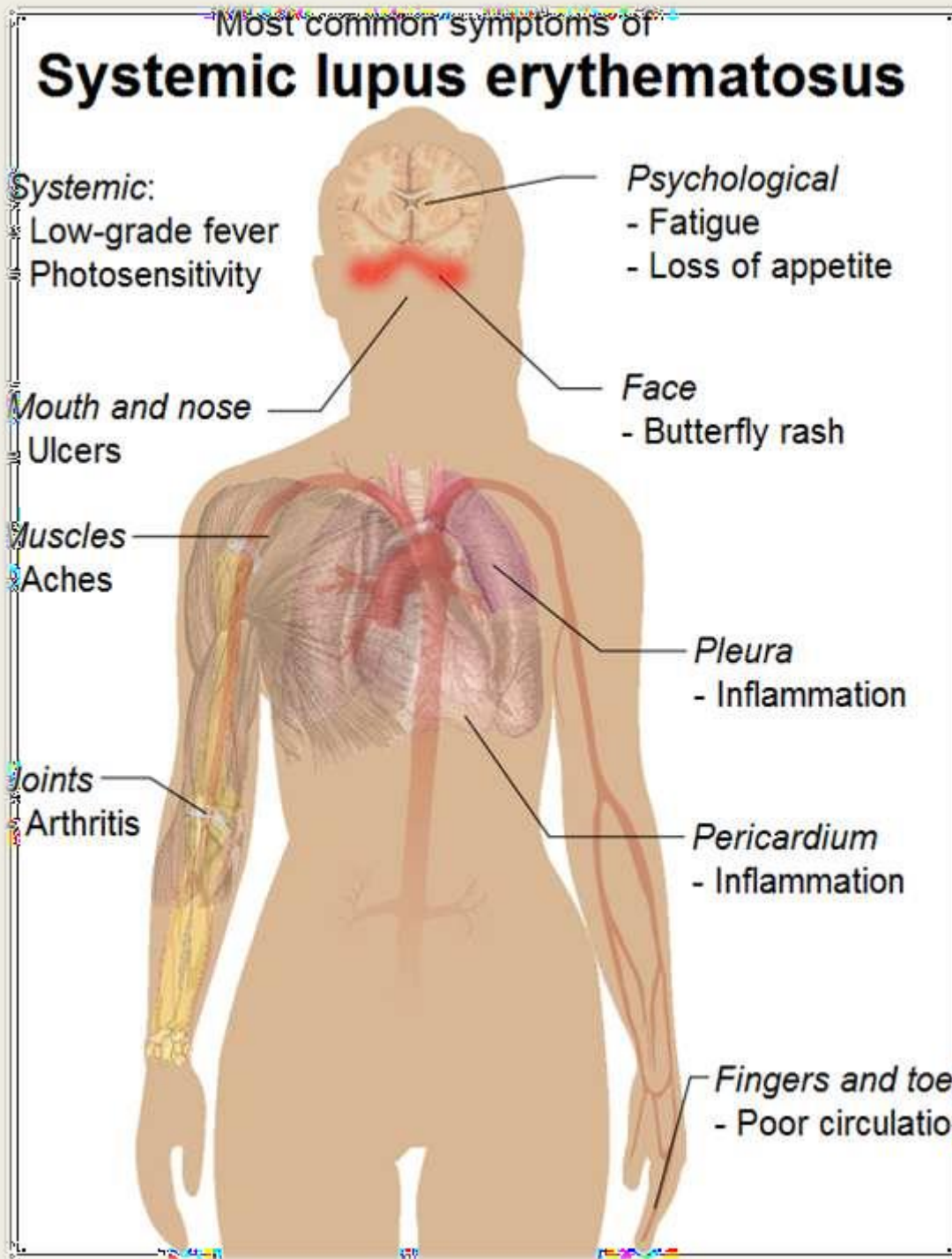
Muscles
- Aches

Pleura
- Inflammation

Joints
- Arthritis

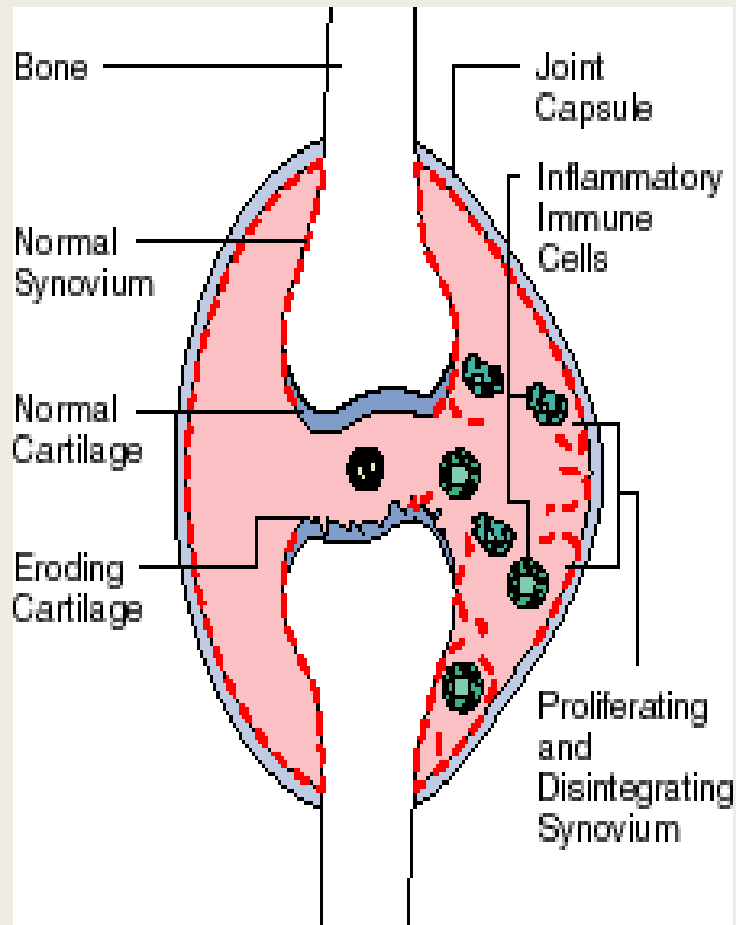
Pericardium
- Inflammation

Fingers and toes
- Poor circulation



Rheumatoid Arthritis

- Disease of the joints.
- Caused by the auto Antibody of IgM type, called as rheumatoid factors.
- The synovial fluid of these patients contain increased no. of T-cells & macrophages.
- Marked by inflammatory changes in the synovial membrane.
- In later stage, deformity develops.



Condition of Rheumatoid Arthritis

HLA & Disease

- Major histocompatibility complex (MHC) in humans .
- This group of genes resides on chromosome 6.
- HLAs belongs to **MHC class I** present peptide from inside the cell which are degraded by proteasomes.

- HLAs corresponding to MHC class II present antigens from outside of the cell to T-lymphocytes.
- HLAs corresponding to MHC class III encode components of the complement system.

Role of HLA

1. In infectious disease
2. In graft rejection
3. In autoimmunity
4. In cancer

Autoimmune diseases linked to HLA types

- **Diabetes**
- **Graves' disease**
- **Hashimoto's thyroiditis**
- **Lupus**
- **Multiple Sclerosis**
- **Myasthenia gravis**
- **Rheumatoid Arthritis**

Immunosuppressive Drugs

- Drugs that inhibit or prevent activity of the immune system.
- They are used in immunosuppressive therapy to:
 - **Prevent** **the rejection** of transplanted organs and tissues (e.g., bone marrow, heart, kidney, liver)
 - **Treat** **autoimmune** **diseases** (e.g., rheumatoid arthritis, multiple

- Immunosuppressive drugs can be classified into four groups:
 - **Glucocorticoids** (suppress allergic, inflammatory and autoimmune disorders) .
 - **Cytostatics** (inhibit cell division) .
 - **Antibodies** (prevent the acute rejection and targeted treatment of or autoimmune disorders) .
 - **Drugs acting on immunophilins** (Ciclosporin, Tacrolimus) .

Treatment

- The key to treating autoimmunity is immunomodulation .
- Some autoimmune diseases are treated with medications that enhance specific symptoms.
- **Haemolytic anaemia:** Treated with Vit B₁₂
- **SLE :** Treated with nonsteroidal anti-inflammatory drugs such as ibuprofen or naproxen, antimalarial drugs, and corticosteroids.
 - In more aggressive cases, immunosuppressive drugs may be used.

Mouse Models

Human Disease

Mouse Models

Rheumatoid Arthritis

Collagen Induced Arthritis
(CIA)

Multiple Sclerosis

Experimental Autoimmune
Encephalitis (EAE)

Diabetes

Non Obese Diabetic (NOD)

Lupus

MRL^{lpr}