Autoimmunity

Dr. Shanmugaapriya
Assistant Professor
Department of Biomedical Science
Bharathidasan University
Trichy-24

Immune Tolerance - Essential?

Autoimmunity

- Break down of mechanism -induce tolerance to self antigens - autoimmunity

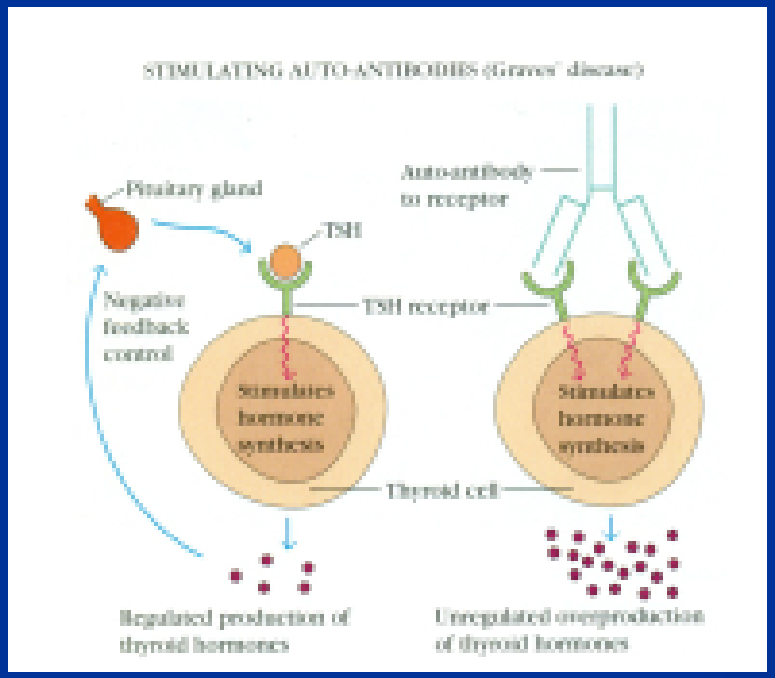
Classification

- Based on the organ or tissue involved
  - Organ-specific –
    - IR directed against antigens associated with the target organ
  - Non-organ-specific –
    - IR directed against an antigen not associated with the target organ

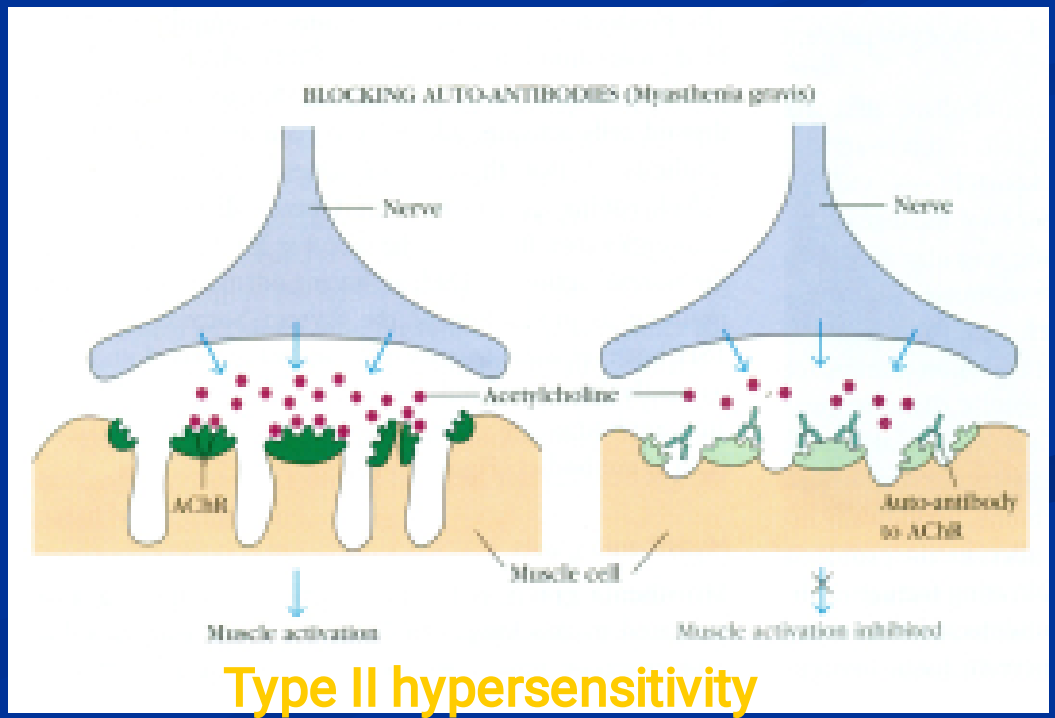
Effector mechanisms in autoimmune diseases

Antibodies -Direct effect

Agonist



Antagonist

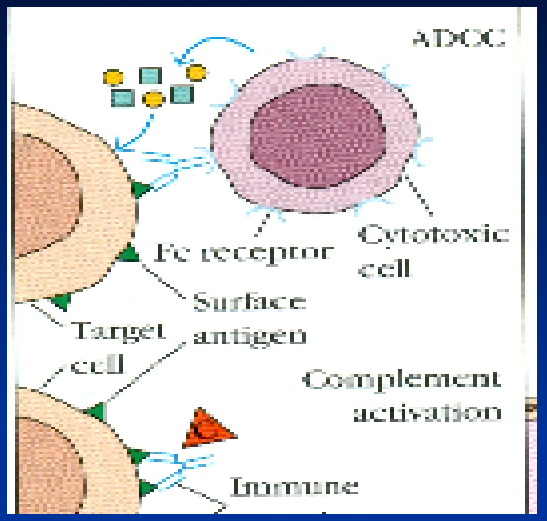


Type II hypersensitivity

Figure from Kuby Immunology

Type II hypersensitivity

- Autoimmune hemolytic anemia



Type III hypersensitivity

- SLE
- RA
- Goodpasture's syndrome
- Poststreptococcal glomerulonephritis

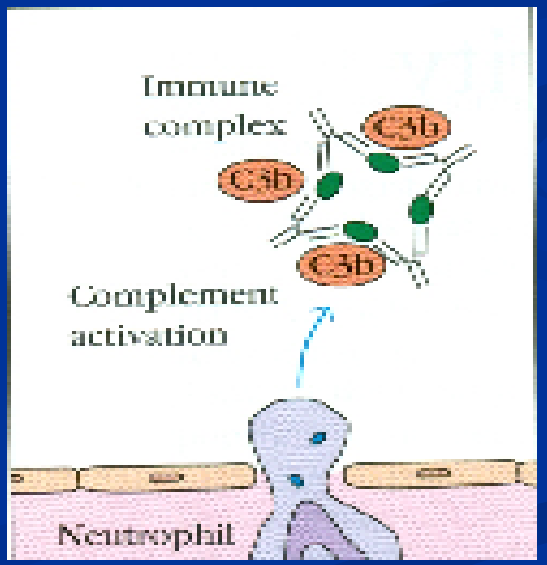


Figure from Kuby Immunology

Cell-mediated damage

- Major cells
  - phagocytic macrophages,
  - neutrophils,
  - self-reactive CD4+T helper cells
  - self-reactiveCD8+cytolytic T cells

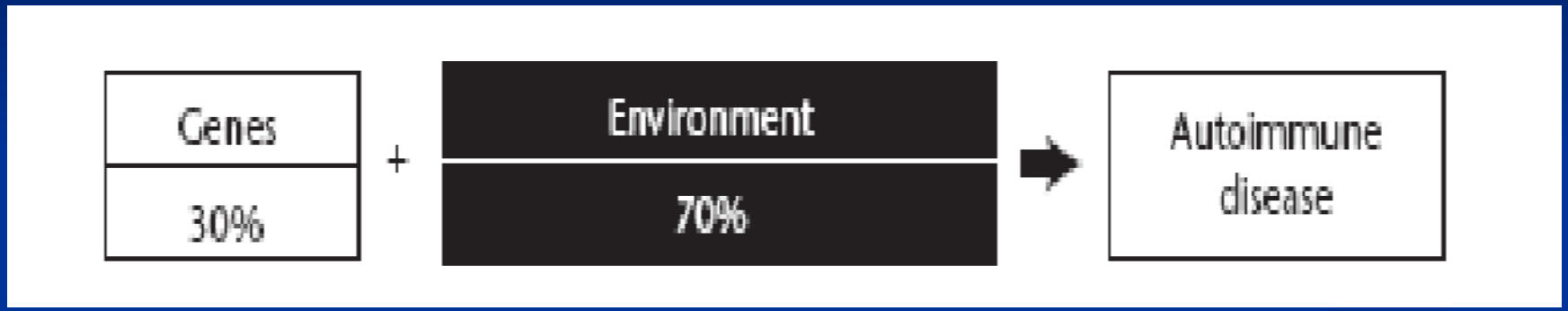
- Minor role
  - natural killer cells
  - mast cells
  - dendritic cells

Effector mechanisms in autoimmune diseases

Disease	Self antigen	Immune response
	ORGAN-SPECIFIC AUTOIMMUNE DISEASES	
Addison's disease	Adrenal cells	Auto-antibodies
Autoimmune hemolytic anemia	RBC membrane proteins	Auto-antibodies
Goodpasture's syndrome	Renal and lung basement membranes	Auto-antibodies
Graves' disease	Thyroid-stimulating hormone receptor	Auto-antibody (stimulating)
Hashimoto's thyroiditis	Thyroid proteins and cells	T_H1 cells, auto-antibodies
Idiopathic thrombocyopenia purpura	Platelet membrane proteins	Auto-antibodies
Insulin-dependent diabetes mellitus	Pancreatic beta cells	T_H1 cells, auto-antibodies
Myasthenia gravis	Acetylcholine receptors	Auto-antibody (blocking)
Myocardial infarction	Heart	Auto-antibodies
Pernicious anemia	Gastric parietal cells; intrinsic factor	Auto-antibody
Poststreptococcal glomerulonephritis	Kidney	Antigen-antibody complexes
Spontaneous infertility	Sperm	Auto-antibodies
	SYSTEMIC AUTOIMMUNE DISEASES	
Ankylosing spondylitis	Vertebrae	Immune complexes
Multiple sclerosis	Brain or white matter	T_H1 cells and T_C cells, auto-antibodies
Rheumatoid arthritis	Connective tissue, IgG	Auto-antibodies, immune complexes
Scleroderma	Nuclei, heart, lungs, gastrointestinal tract, kidney	Auto-antibodies
Sjögren's syndrome	Salivary gland, liver, kidney, thyroid	Auto-antibodies
Systemic lupus erythematosus (SLE)	DNA, nuclear protein, RBC and platelet membranes	Auto-antibodies, immune complexes

Table 16-1
Kuby IMMUNOLOGY, Sixth Edition

Etiology of autoimmune diseases



INFECTIOUS AGENTS

NON-INFECTIOUS AGENTS

Genetic Susceptibility To Autoimmunity

- Epidemiologic studies
  - Genetic factors are crucial determinants
- Familial clustering
  - Hashimoto's thyroiditis (first degree relatives)
  - Pernicious anemia
- Studies in twins
  - rate of concordance is higher in monozygotic than in dizygotic twins

- Linkage analysis
  - MHC complex
  - Candidate loci for susceptibility
    - cytokines,
    - cytokine receptors
    - other immunoregulatory molecules

HLA alleles & Autoimmune Disease

Disease	HLA allele
Ankylosing spondylitis	**B27**
Goodpasture's syndrome	DR2
Graves's disease	B8/DR5
Juvenile rheumatoid arthritis	B27/DR5
Multiple sclerosis	DR2
Myasthenia gravis	DR3
Rheumatoid arthritis	DW4/DR4
Sjogren's syndrome	DW3
Systemic lupus erythematosus	DR3
Ulcerative colitis	**B5**
Pernicious anemia	DR5

- HLA Allelic variation in different individuals accounts functional differences
  - by differential ability to bind
  - by differential ability in displaying antigeneic peptides

Non-HLA genes

- Functional polymorphisms or mutations / tolerance induction
- SNP or microsatellites - promoter / other regulatory regions of genes
- Functions
  - affect the amount of protein produced
  - the degree of receptor expression
  - their functional ability to bind their ligands
  - strength of their immune response

- Cytokines
- CTLA-4
- FOX-P3
- FAS, FASL & Bcl2

- Cytokines gene polymorphisms
  - Inter-individual differences in cytokine production
  - mechanism for the alteration of the TH1/TH2 balance
  - efficient functioning of the immune system thus contributing for the clinical course and outcome of many immune diseases

Infectious Agents

- Potential to initiate autoreactivity through
  - Molecular mimicry
  - Polyclonal activation
  - Release of previously sequestered antigens
  - Cytokine imbalance