

# Systemic Lupus Erythematosus Overview

Supplementary Materials



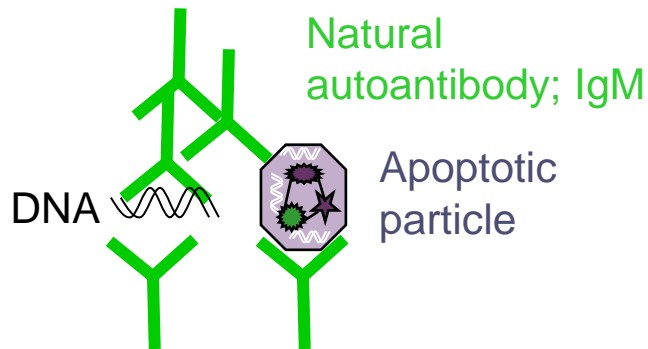
the  
**upus**  
initiative  
Eliminating Health Disparities in Lupus

Eliminating health disparities • Cultural competence • Genetic and non-genetic factors • Health equity • Signs and symptoms of disease onset • Complex disease • Social determinants • Interdisciplinary care • Early diagnosis • Dermatologic • Early diagnosis • Cardiovascular • Pulmonary • Neurologic • Reproductive • Signs and symptoms of disease onset • Complex disease • Dermatologic • Early diagnosis • Genetic factors • Pulmonary • Renal • Dermatologic • Psychosocial • Cardiovascular • Renal • Cultural competence • Genetic and non-genetic factors • Health equity • Signs and symptoms of disease onset • Cardiovascular • Reproductive • Renal

# Autoantibodies

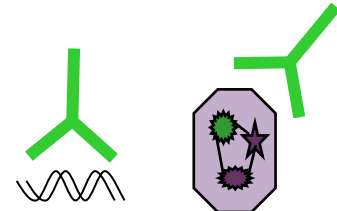
- **Natural autoantibodies** effectively clear cellular debris (IgM) in healthy individuals
- **Pathogenic autoantibodies:**
  - IgG
  - Form immune complexes
  - Directly target cells through cross-reactivity with other antigens. For example, subsets of anti-dsDNA antibodies bind NMDA receptors on neurons or components of the basement membrane in renal glomeruli

# Beneficial Autoantibodies

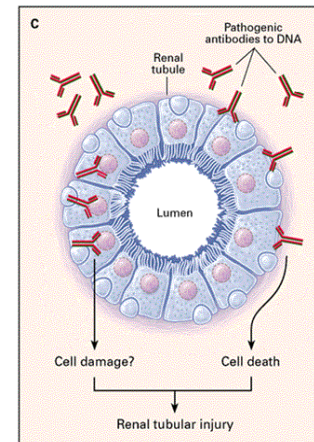
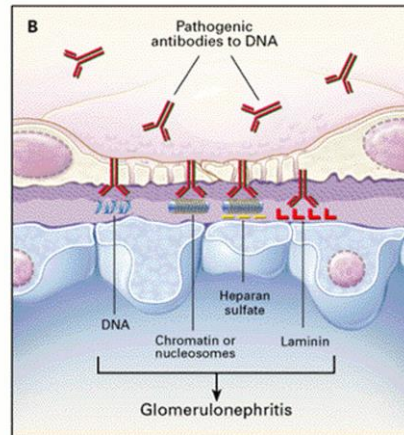
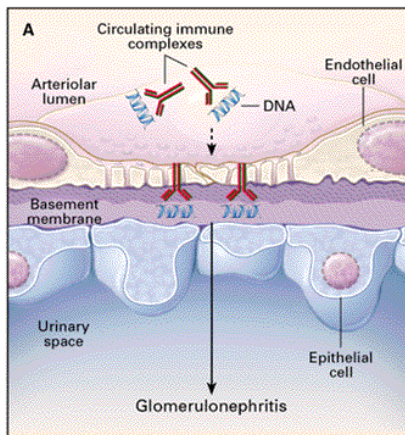


Cleared by natural IgM, complement, DNase and SAP

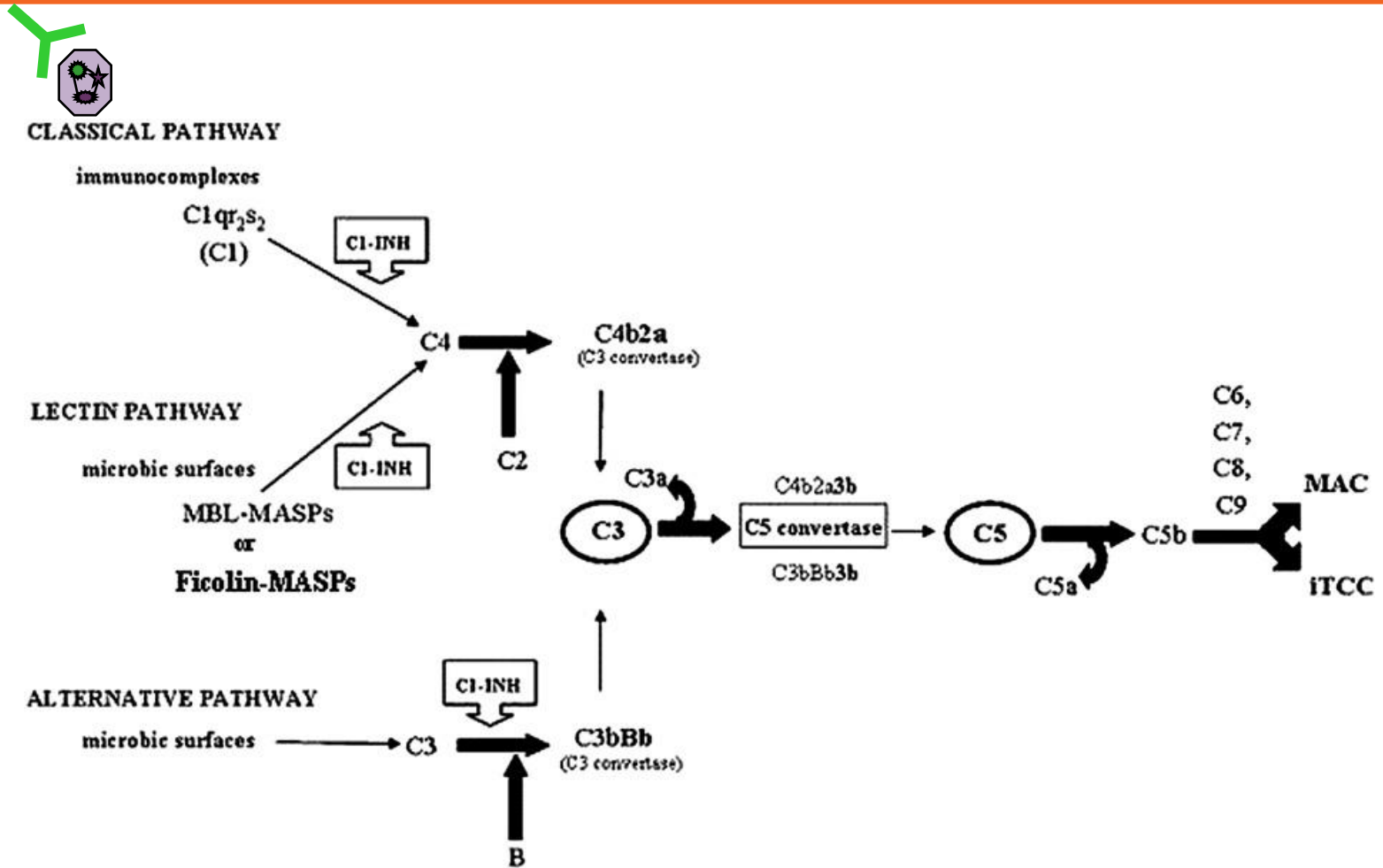
*Deficiencies cause SLE*



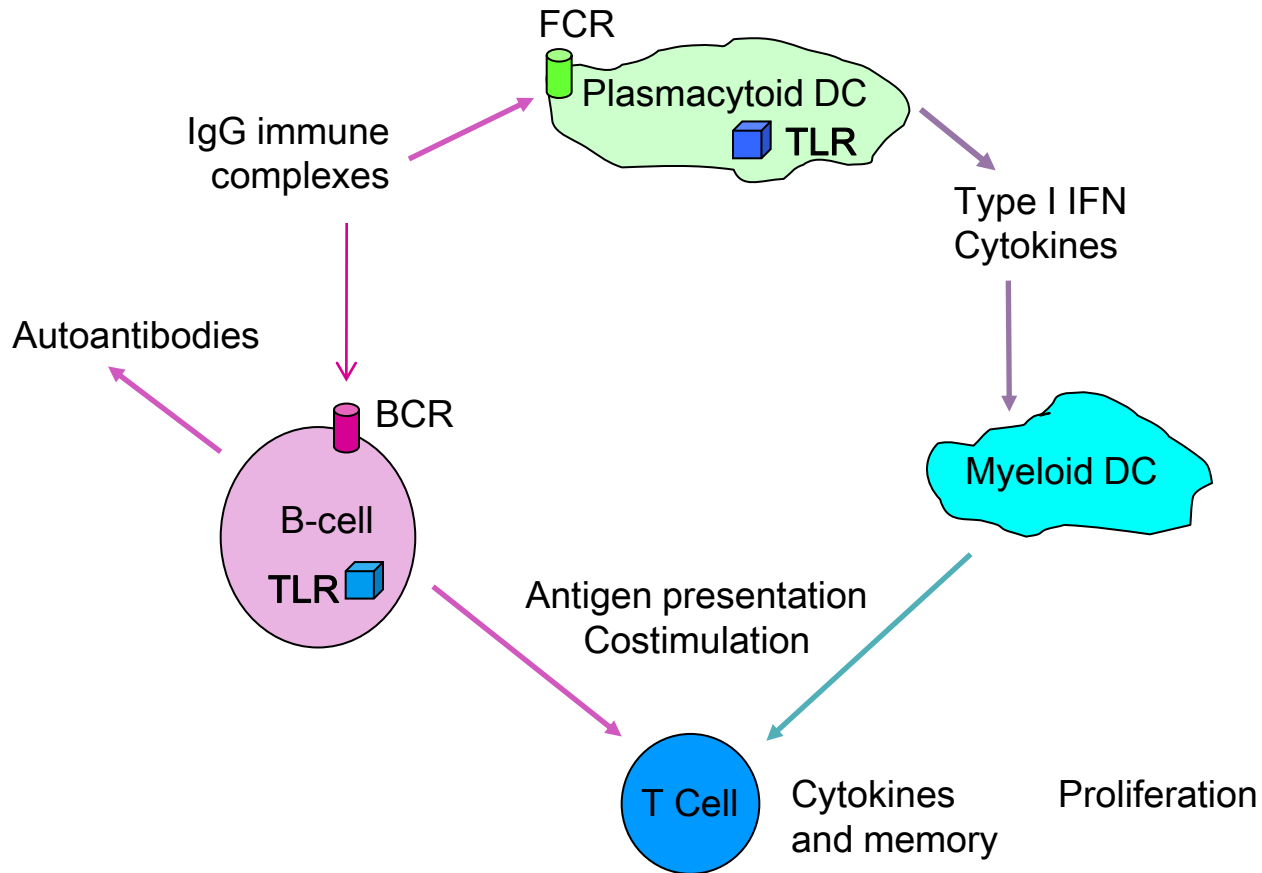
## Pathogenic Autoantibodies: anti-dsDNA



# Complement Activation



# DNA-Containing Immune Complexes Activate Dendritic Cells and Autoreactive B-Cells



IgM immune complexes do **not** activate DCs or B-cells

# Immune Dysregulation—T-Cells

- Activated T-cells provide support to autoreactive B-cells and facilitate autoantibody production
- SLE patients exhibit increased numbers of Th17 and Th cells and decreased numbers of Tregs
- Lupus T-cells are less susceptible to activation-induced cell death
- Alterations in the TCR complex (the TCR  $\zeta$  chain) lead to changes in intracellular signaling that result in increased expression of CD40L and decreased production of IL-2

# Immune Dysregulation—Plasmacytoid Dendritic Cells

- **Activated plasmacytoid dendritic cells (pDC)**
  - Produce large amounts of IFN- $\alpha$
  - Stimulate activation and proliferation of autoreactive T- and B-cells
  - Different types of DCs activate different T-cell subsets; Th1, Th2, Th17, and Treg (dependent on cytokine milieu)

# Signs and Symptoms

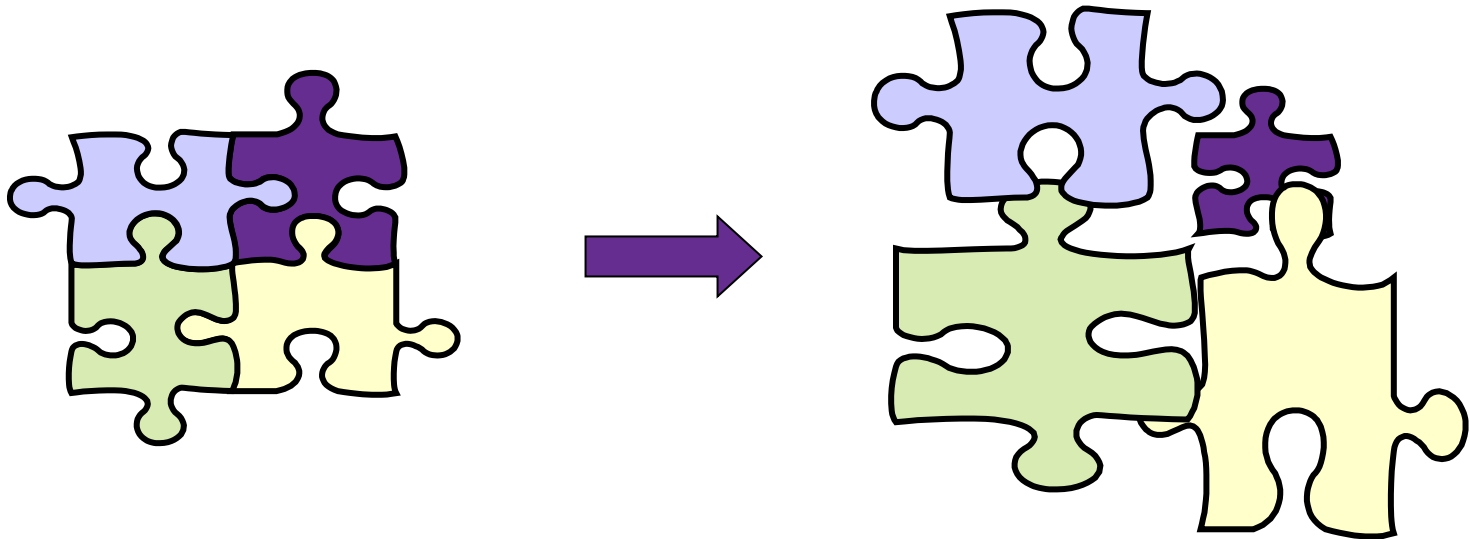
Symptoms Occurrence (ever)	
Arthralgias	95%
Neurologic	90%
Fever >100 °F (38 °C)	90%
Prolonged or extreme fatigue	81%
Arthritis	80%
Skin rashes	74%
Anemia	71%
Kidney involvement	50%
Pleurisy and/or pericarditis	45%
Butterfly-shaped rash across the cheeks and nose	42%
Sun or light sensitivity (photosensitivity)	30%
Hair loss	27%
Abnormal blood clotting problems	20%
Raynaud's phenomenon	17%
Seizures	15%
Mouth or nose ulcers	12%



# Autoimmunity—Jigsaw Model

## ***Current proposal:***

Altered immune homeostasis leads to simultaneous autoreactivity, immunodeficiency, and malignancy



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# Bibliography

**Slide 3 Reference**

Hahn HB. Antibodies to DNA. *N Engl J Med.* 1998;338:1359-1368.

**Slide 4 Reference**

Chen M, Daha MR, Kallenberg CG. The complement system in systemic autoimmune disease. *J Autoimmun.* 2010;34:J276-J286.