

Systemic Lupus Erythematosus Overview

Supplementary Materials

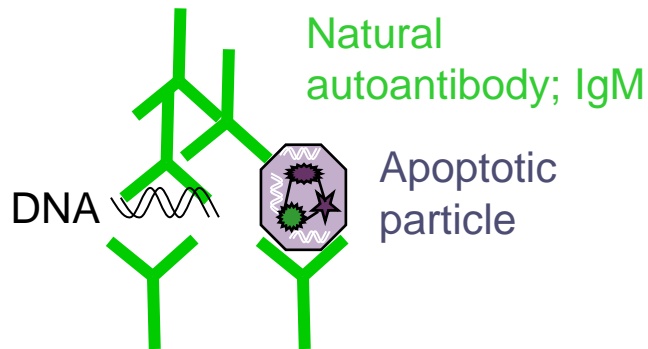


Eliminating health disparities • Cultural competence • Genetic and non-genetic factors • Health equity • Signs and symptoms of disease onset • Complex disease • Social determinants • Interdisciplinary care • Early diagnosis • Dermatologic • Early diagnosis • Cardiovascular • Pulmonary • Neurologic •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

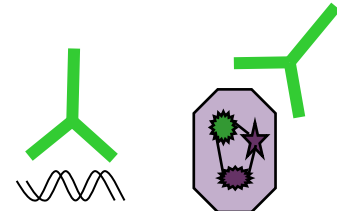
- **Natural autoantibodies** effectively clear cellular debris (IgM) in healthy individuals
- **Pathogenic autoantibodies:**
 - IgG
 - Form immune complexes
 - Directly target cells through cross-reactivity with other antigens. For example, subsets of anti-dsDNA antibodies bind NMDA receptors on neurons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

Beneficial Autoantibodies

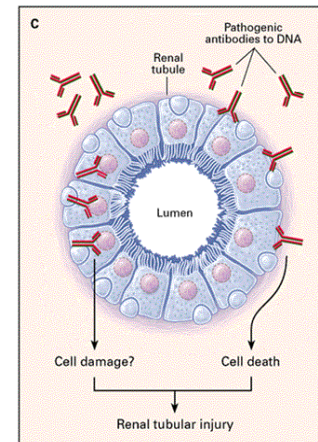
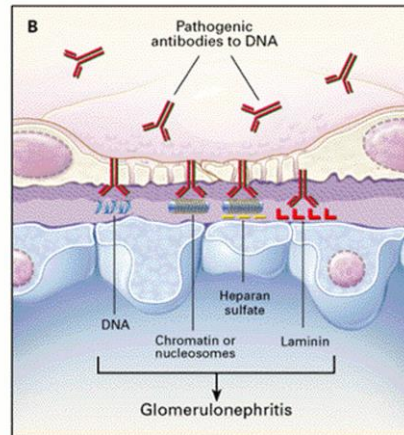
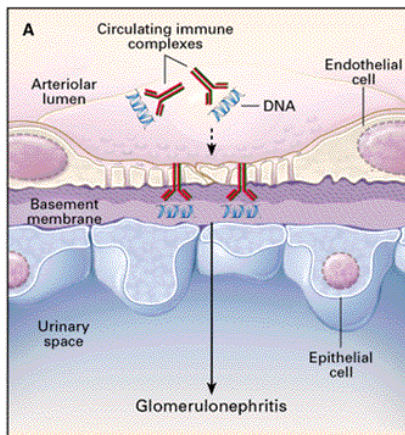


Cleared by natural IgM, complement, DNase and SAP

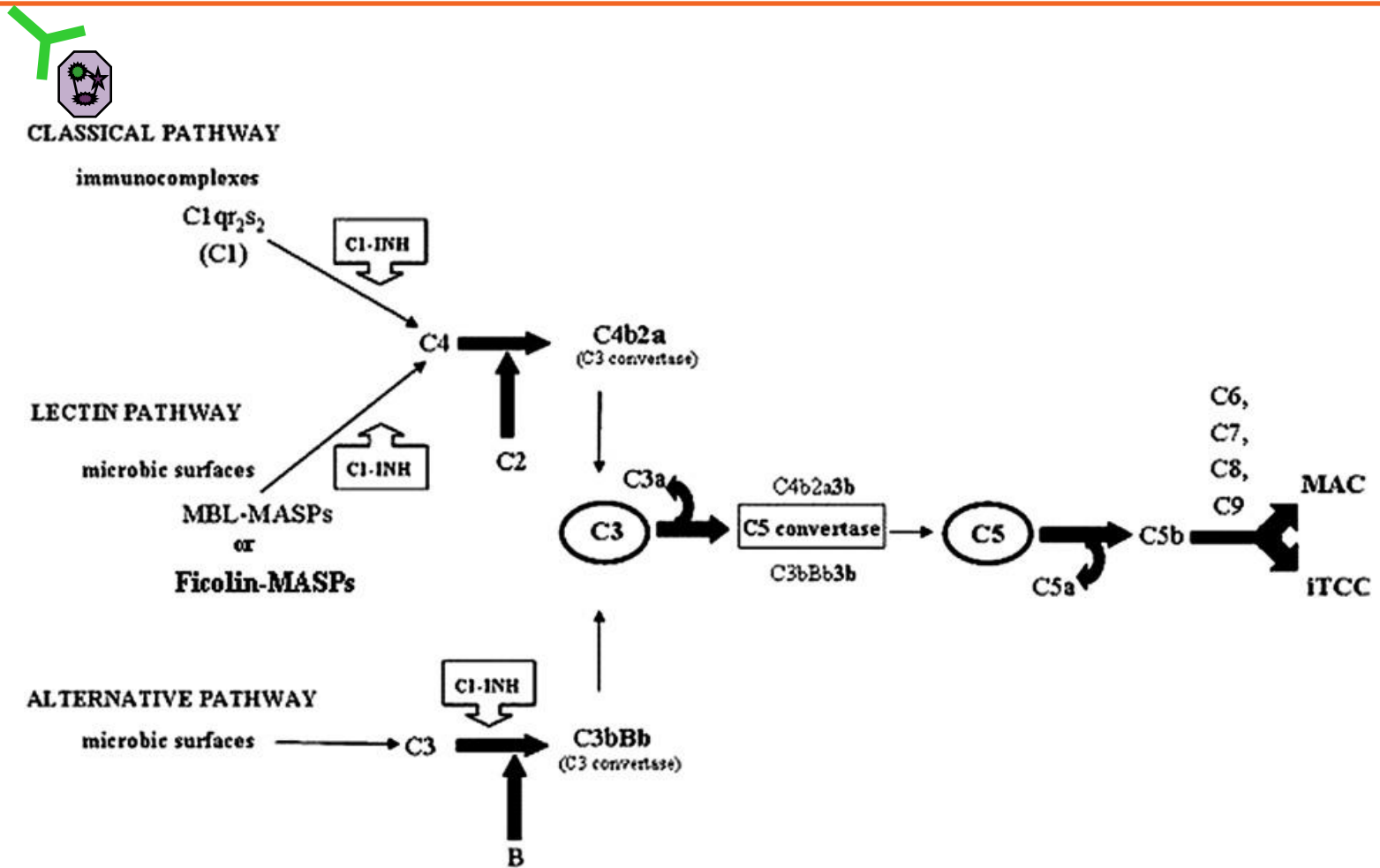
Deficiencies cause SLE



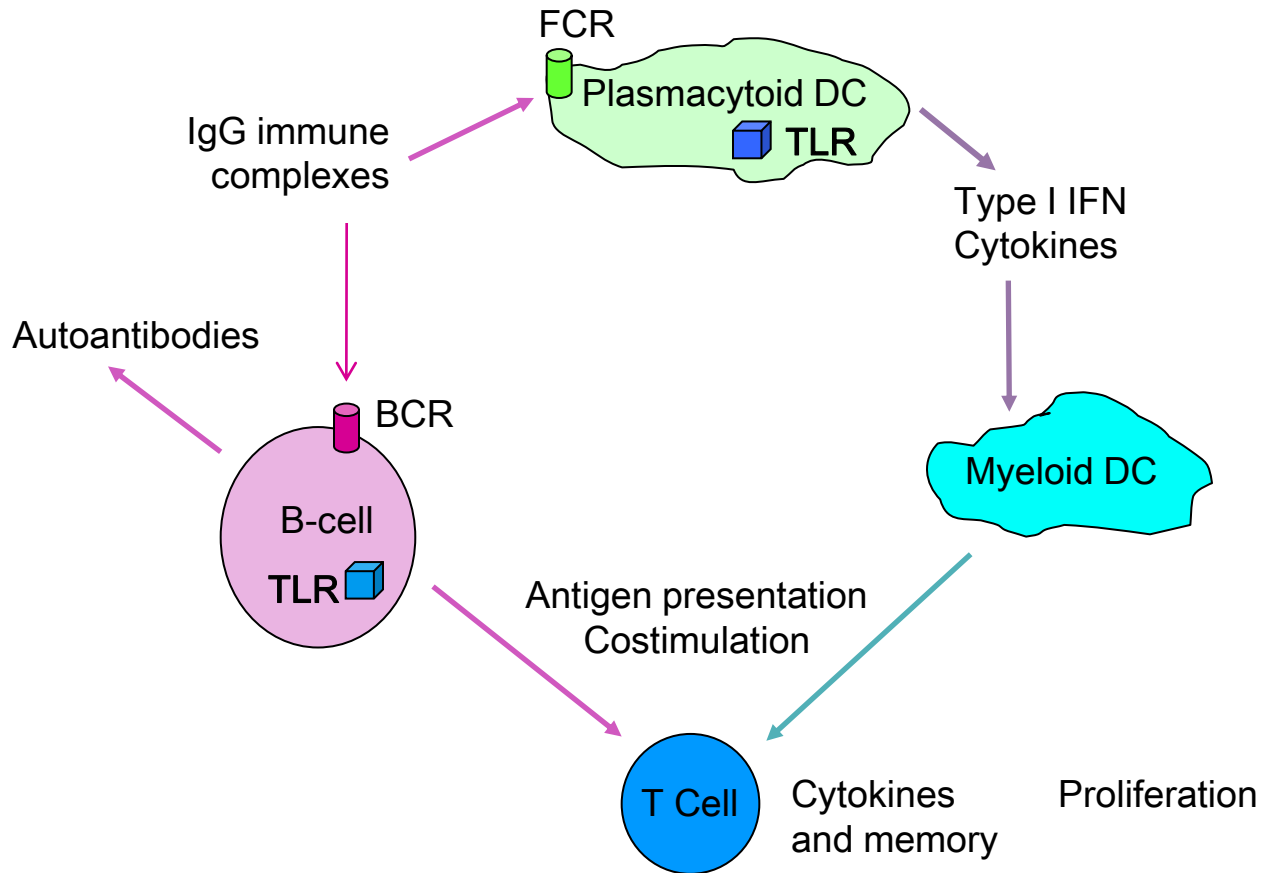
Pathogenic Autoantibodies: anti-dsDNA



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 ζ 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- α
 - 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)

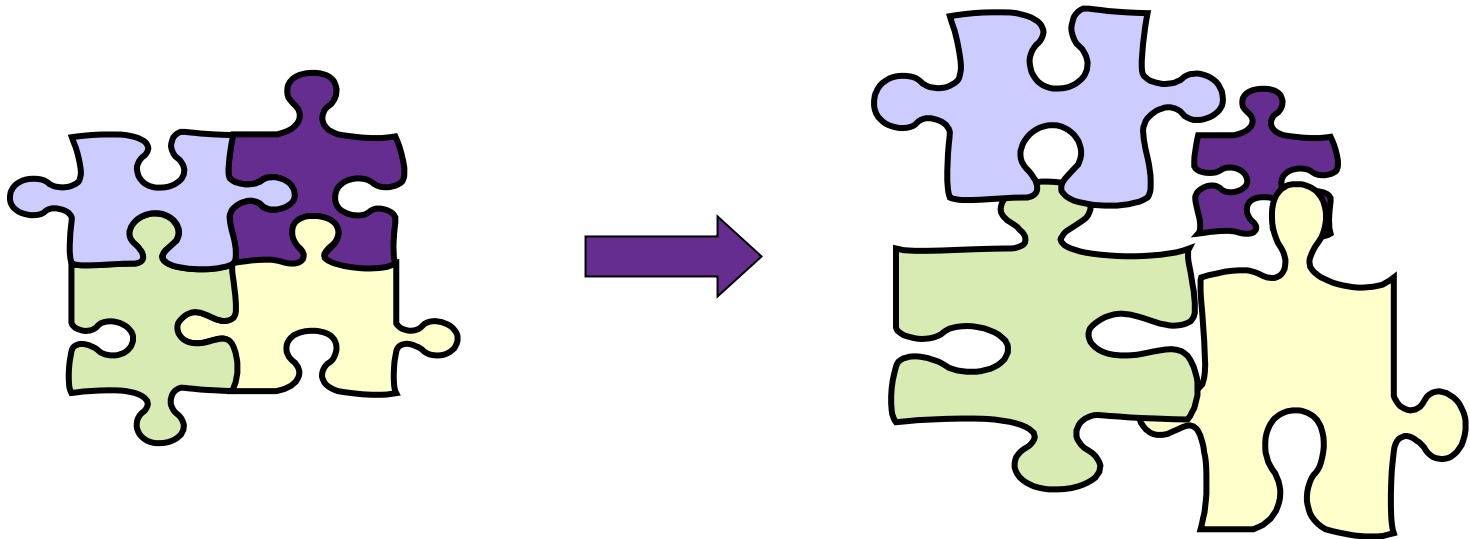
Signs and Symptoms

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



Bibliography

Slide 3 Reference

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

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