in the type 1 interferon pathway are very strongly associated with the development of SLE.

## ■ IMMUNOPATHOGENIC MECHANISMS IN AUTOIMMUNE DISEASES

The mechanisms of tissue injury in autoimmune diseases can be divided into antibody-mediated and cell-mediated processes. Representative examples are listed in **Table 355-3**.

**TABLE 355-3 Mechanisms of Tissue Damage in Autoimmune Disease**

| EFFECTOR | MECHANISM | TARGET | DISEASE |
|---|---|---|---|
| Autoantibody | Blocking or inactivation | α Chain of the nicotinic acetylcholine receptor | Myasthenia gravis |
| | | Phospholipid–$\beta_2$-glycoprotein I complex | Antiphospholipid syndrome |
| | | Insulin receptor | Insulin-resistant diabetes mellitus |
| | | Intrinsic factor | Pernicious anemia |
| | Stimulation | TSH receptor (LATS) | Graves' disease |
| | | Proteinase-3 (ANCA) | Granulomatosis with polyangiitis |
| | | Epidermal cadherin | Pemphigus vulgaris |
| | | Desmoglein 3 | |
| | Complement activation | $\alpha_3$ Chain of collagen IV | Goodpasture's syndrome |
| | Immune complex formation | Double-stranded DNA | Systemic lupus erythematosus |
| | | Immunoglobulin | Rheumatoid arthritis |
| | Opsonization | Platelet GpIIb:IIIa | Autoimmune thrombocytopenic purpura |
| | | Rh antigens, I antigen | Autoimmune hemolytic anemia |
| | Antibody-dependent cellular cytotoxicity | Thyroid peroxidase, thyroglobulin | Hashimoto's thyroiditis |
| T cells | Cytokine production | | Rheumatoid arthritis, multiple sclerosis, type 1 diabetes mellitus |
| | Cellular cytotoxicity | | Type 1 diabetes mellitus |

*Abbreviations:* ANCA, antineutrophil cytoplasmic antibody; LATS, long-acting thyroid stimulator; TSH, thyroid-stimulating hormone.

The pathogenicity of autoantibodies can be mediated through several mechanisms, including opsonization of soluble factors or cells, activation of an inflammatory cascade via the complement system, and interference with the physiologic function of soluble molecules or cells or immune complex–mediated activation of cells through engagement of activating Fc receptors.

In autoimmune thrombocytopenic purpura, opsonization of platelets targets them for elimination by phagocytes. Likewise, in autoimmune hemolytic anemia, binding of immunoglobulin to red cell membranes leads to phagocytosis and lysis of the opsonized cell. Goodpasture's syndrome, a disease characterized by lung hemorrhage and severe glomerulonephritis, represents an example of antibody binding leading to local activation of complement and