TABLE 372e-15 TRAFFICKING MOLECULES INVOLVED IN INFLAMMATORY DISEASE PROCESSES

		Proposed Leukocyte Receptors for Endothelial Traffic Signals		
Disease	**Key Effector Cell**	**L-Selectin, Ligand**	**GPCR**	**Integrin[a]**
Acute Inflammation				
Myocardial infarction	Neutrophil	PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
Stroke	Neutrophil	L-Selectin, PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
Ischemia-reperfusion	Neutrophil	PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
T_H1 Inflammation				
Atherosclerosis	Monocyte	PSGL-1	CCR1, CCR2, BLT1, CXCR2, CX3CR1	VLA-4
	T_H1	PSGL-1	CXCR3, CCR5	VLA-4
Multiple sclerosis	T_H1	PSGL-1 (?)	CXCR3, CXCR6	VLA-4, LFA-1
	Monocyte	PSGL-1 (?)	CCR2, CCR1	VLA-4, LFA-1
Rheumatoid arthritis	Monocyte	PSGL-1	CCR1, CCR2	VLA-1, VLA-2, VLA-4, LFA-1
	T_H1	PSGL-1	CXCR3, CXCR6	VLA-1, VLA-2, VLA-4, LFA-1
	Neutrophil	L-Selectin, PSGL-1	CXCR2, BLT1	LFA-1[b]
Psoriasis	Skin-homing T_H1	CLA	CCR4, CCR10, CXCR3	VLA-4[c], LFA-1
Crohn's disease	Gut-homing T_H1	PSGL-1	CCR9, CXCR3	α4, β7, LFA-1
Type 1 diabetes	T_H1	PSGL-1 (?)	CCR4, CCR5	VLA-4, LFA-1
	CD8	L-Selectin (?), PSGL-1 (?)	CXCR3	VLA-4, LFA-1
Allograft rejection	CD8	PSGL-1	CXCR3, CX3CR1, BLT1	VLA-4, LFA-1
	B cell	L-Selectin, PSGL-1	CXCR5, CXCR4	VLA-4, LFA-1
Hepatitis	CD8	PSGL-1	CXCR3, CCR5, CXCR6	VLA-4
Lupus	T_H1	None	CXCR6	VLA-4[d]
	Plasmacytoid DC	L-Selectin, CLA	CCR7, CXCR3, ChemR23	LFA-1, Mac-1
	B cell	CLA (?)	CXCR5, CXCR4	LFA-1
T_H2 Inflammation				
Asthma	T_H2	PSGL-1	CCR4, CCR8, BLT1	LFA-1
	Eosinophil	PSGL-1	CCR3, PAFR, BLT1	VLA-4, LFA-1
	Mast cells	PSGL-1	CCR2, CCR3, BLT1	VLA-4, LFA-1
Atopic dermatitis	Skin-homing T_H2	CLA	CCR4, CCR10	VLA-4, LFA-1

[a]Various β_1 integrins have been linked in different ways in basal lamina and interstitial migration of distinct cell types and inflammatory settings. [b]In some settings, Mac-1 has been linked to transmigration. [c]CD44 can act in concert with VLA-4 in particular models of leukocyte arrest. [d]T_H2 cells require VAP-1 to traffic to inflamed liver.

Source: From AD Luster et al: Nat Immunol 6:1182, 2005; with permission from Macmillan Publishers Ltd. Copyright 2005.

TABLE 372e-16 COMPLEMENT DEFICIENCIES AND ASSOCIATED DISEASES

Component	Associated Diseases
Classic Pathway	
Clq, Clr, Cls, C4	Immune-complex syndromes,[a] pyogenic infections
C2	Immune-complex syndromes,[a] few with pyogenic infections
C1 inhibitor	Rare immune-complex disease, few with pyogenic infections
C3 and Alternative Pathway C3	
C3	Immune-complex syndromes,[a] pyogenic infections
D	Pyogenic infections
Properdin	*Neisseria* infections
I	Pyogenic infections
H	Hemolytic-uremic syndrome
Membrane Attack Complex	
C5, C6, C7, C8	Recurrent *Neisseria* infections, immune-complex disease
C9	Rare *Neisseria* infections

[a]Immune-complex syndromes include systemic lupus erythematosus (SLE) and SLE-like syndromes, glomerulonephritis, and vasculitis syndromes.

Source: After JA Schifferli, DK Peters: Lancet 322:957, 1983. Copyright 1983, with permission from Elsevier.

Immediate-Type Hypersensitivity Helper T cells that drive antiallergen IgE responses are usually T_H2-type inducer T cells that secrete IL-4, IL-5, IL-6, and IL-10. Mast cells and basophils have high-affinity receptors for the Fc portion of IgE (FcRI), and cell-bound antiallergen IgE effectively "arms" basophils and mast cells. Mediator release is triggered by antigen (allergen) interaction with Fc receptor-bound IgE, and the mediators released are responsible for the pathophysiologic changes of *allergic diseases* (Table 372e-11). Mediators released from mast cells and basophils can be divided into three broad functional types: (1) those that increase vascular permeability and contract smooth muscle (histamine, platelet-activating factor, SRS-A, BK-A), (2) those that are chemotactic for or activate other inflammatory cells (ECF-A, NCF, leukotriene B_4), and (3) those that modulate the release of other mediators (BK-A, platelet-activating factor) (Chap. 376).

Cytotoxic Reactions of Antibody In this type of immunologic injury, complement-fixing (C1-binding) antibodies against normal or foreign cells or tissues (IgM, IgG1, IgG2, IgG3) bind complement via the classic pathway and initiate a sequence of events similar to that initiated by immune-complex deposition, resulting in cell lysis or tissue injury. Examples of antibody-mediated cytotoxic reactions include red cell lysis in *transfusion reactions*, *Goodpasture's syndrome* with anti–glomerular basement membrane antibody formation, and *pemphigus vulgaris* with antiepidermal antibodies inducing blistering skin disease.

Classic Delayed-Type Hypersensitivity Reactions Inflammatory reactions initiated by mononuclear leukocytes and not by antibody alone have