TABLE 372e-6 DISEASES ASSOCIATED WITH INFLAMMASOME ACTIVITY

Disease	Clinical Features	Gene Mutated	Etiologic Agent	Inflammasome Involvement	Anakinra Response[a]
Familial cold autoinflammatory syndrome (FCAS)	Fever, arthralgia, cold-induced urticaria	*NALP3*		Overactive	Yes
Muckle-Wells syndrome (MWS)	Fever, arthralgia, urticaria, sensorineural deafness, amyloidosis	*NAPL3*		Overactive	Yes
Chronic infantile neurologic cutaneous and articular syndrome (CINCA, NOMID)	Fever, severe arthralgia, urticaria, neurologic problems, severe amyloidosis	*NALP3*		Overactive	Yes
Familial Mediterranean fever (FMF)	Fever, peritonitis, pleuritis, amyloidosis	Pyrin		Overactive	Partial
Pyogenic arthritis, pyoderma gangrenosum, and acne syndrome (PAPA)	Pyogenic sterile arthritis	*PSTPIP1*		Overactive	Yes
Hyperimmunoglobulin D syndrome (HIDS)	Arthralgia, abdominal pain, lymphadenopathy	Mevalonate kinase		To be demonstrated	Yes
Tumor necrosis factor receptor-1–associated syndrome (TRAPS)	Fever, abdominal pain, skin lesions	*TNF-R1*		To be demonstrated	Yes
Systemic-onset juvenile idiopathic arthritis (SOJIA)	Chronic joint inflammation		Unknown	To be demonstrated	Yes
Adult-onset Still's disease (AOSD)	Arthralgia, fever		Unknown	To be demonstrated	Yes
Behçet's disease	Arthralgia, uveitis, ulcers		Unknown	To be demonstrated	Yes
Schnitzler's syndrome	Urticaria, fever, arthralgia		Unknown	To be demonstrated	Yes
Gout	Metabolic arthritis, pain		Uric acid (MSU)	Activated	Yes
Pseudogout	Arthritis		CPPD	Activated	Yes
Contact dermatitis	Urticaria		Irritants	Activated	Unknown
Fever syndrome	Fever	*NALP12*		Unknown	Unknown
Hydatidiform mole	Hydatid mole	*NALP7*		Unknown	Unknown
Vitiligo	Skin depigmentation, autoimmunity	*NLRP1*		Overactive	Unknown
Crohn's disease		*NLRP3*		Underactive	Unknown
Multiple Sclerosis		*NLPR3*		Activated	Unknown
Psoriasitic arthritis		*NLRP3*		Activated	Yes

[a]Anakinra is a recombinant interleukin-1 (IL-1) receptor antagonist that functions to block the biologic activity of naturally occurring IL-1.

Abbreviation: CPPD, calcium pyrophosphate dehydrate.

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Neutrophils, Eosinophils, and Basophils Granulocytes are present in nearly all forms of inflammation and are amplifiers and effectors of innate immune responses (Figs. 372e-2 and 372e-3). Unchecked accumulation and activation of granulocytes can lead to host tissue damage, as seen in neutrophil- and eosinophil-mediated *systemic necrotizing vasculitis*. Granulocytes are derived from stem cells in bone marrow. Each type of granulocyte (neutrophil, eosinophil, or basophil) is derived from a different subclass of progenitor cell that is stimulated to proliferate by colony-stimulating factors (Table 372e-7). During terminal maturation of granulocytes, class-specific nuclear morphology and cytoplasmic granules appear that allow for histologic identification of granulocyte type.

Neutrophils express Fc receptor IIIa for IgG (CD16) as well as receptors for activated complement components (C3b or CD35). Upon interaction of neutrophils with antibody-coated (opsonized) bacteria or immune complexes, azurophilic granules (containing myeloperoxidase, lysozyme, elastase, and other enzymes) and specific granules (containing lactoferrin, lysozyme, collagenase, and other enzymes) are released, and microbicidal superoxide radicals (O_2^-) are generated at the neutrophil surface. The generation of superoxide leads to inflammation by direct injury to tissue and by alteration of macromolecules such as collagen and DNA.

Eosinophils express Fc receptor II for IgG (CD32) and are potent cytotoxic effector cells for various parasitic organisms. In *Nippostrongylus brasiliensis* helminth infection, eosinophils are important cytotoxic effector cells for removal of these parasites. Key to regulation of eosinophil cytotoxicity to *N. brasiliensis* worms are antigen-specific T helper cells that produce IL-4, thus providing an example of regulation of innate immune responses by adaptive immunity antigen-specific T cells. Intracytoplasmic contents of eosinophils, such as major basic protein, eosinophil cationic protein, and eosinophil-derived neurotoxin, are capable of directly damaging tissues and may be responsible in part for the organ system dysfunction in the *hypereosinophilic syndromes* (Chap. 80). Because the eosinophil granule contains anti-inflammatory types of enzymes (histaminase, arylsulfatase, phospholipase D), eosinophils may homeostatically downregulate or terminate ongoing inflammatory responses.

Basophils and tissue mast cells are potent reservoirs of cytokines such as IL-4 and can respond to bacteria and viruses with antipathogen cytokine production through multiple TLRs expressed on their surface. Mast cells and basophils can also mediate immunity through the binding of antipathogen antibodies. This is a particularly important host defense mechanism against parasitic diseases. Basophils express high-affinity surface receptors for IgE (FcεRII) (CD23) and, upon cross-linking of basophil-bound IgE by antigen, can release histamine, eosinophil chemotactic factor of anaphylaxis, and neutral protease—all mediators of allergic immediate (anaphylaxis) hypersensitivity responses (Table 372e-11). In addition, basophils express surface receptors for activated complement components (C3a, C5a), through