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IUPAC GLOSSARY OF TERMS USED IN IMMUNOTOXICOLOGY

(IUPAC Provisional Recommendations 20XX)

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Abstract: The primary objective of this *Glossary of Terms Used in Immunotoxicology* is to give clear definitions for those who contribute to studies relevant to immunotoxicology but are not themselves immunologists. This applies especially to chemists who need to understand the literature of immunology without recourse to a multiplicity of other glossaries or dictionaries. The Glossary includes terms related to basic and clinical immunology insofar as they are necessary for a self-contained document, and particularly terms related to diagnosing, measuring, and understanding effects of substances on the immune system. The glossary consists of about 1200 terms as primary alphabetical entries, and Annexes of common abbreviations, examples of chemicals with known effects on the immune system, autoantibodies in autoimmune disease, and therapeutic agents used in autoimmune disease and cancer. The authors hope that among the groups who will find this glossary helpful, in addition to chemists, are toxicologists, pharmacologists, medical practitioners, risk assessors, and regulatory authorities. In particular, it should facilitate the worldwide use of chemistry in relation to occupational and environmental risk assessment.

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PREFACE

A major goal of IUPAC is to promote "regulation, standardization, or codification" globally in relevant areas of chemistry. To this end, the Division of Chemistry and Human Health (Division VII), recognizing the importance of toxicology to chemists, produced the Glossary of Terms Used in Toxicology, 2nd ed., in 2007 [1]. That glossary was intended to provide clear and concise definitions for a range of terms in toxicology and toxicokinetics, primarily for chemists who find themselves working in toxicology or requiring a working knowledge of the subject. It was also recognized that other scientists, regulators, and managers must

from time to time interpret toxicological information, and it was hoped that the Glossary would also provide them with ready access to internationally accepted definitions of relevant terms. A number of subspecialties broaden the scope of toxicology, and in 2009 the Division expanded the collection of available definitions with publication of a Glossary of Terms Used in Ecotoxicology [2].

Several years ago the Division initiated a project to evaluate mechanisms by which metals cause immune sensitization in individuals, and subsequently to evaluate critically various immunological tests for their reliability in determining clinical sensitization to various metals. This project resulted in a series of IUPAC technical reports [3-7]. During the course of this work it became evident that immunotoxicology rests upon a specialized vocabulary that incorporates terms from both immunology and toxicology, sometimes combining them in unique ways. Thus it was decided to expand further the list of definitions available to the chemical community and other interested parties by producing a Glossary of Terms Used in Immunotoxicology. The present document is the result. In order to minimize the reader's time in consulting additional texts, terms from [1] were included when it was felt that they were used with particular frequency in immunotoxicology. The authors have also exercised judgment in deciding which terms from basic immunology should be included for the reader's convenience.

In general, American spelling has been adopted for the entry terms, thus hemolytic anemia, edema, and tumor (not haemolytic anaemia, oedema, and tumour). Further, somewhat arbitrary decisions must be made in listing alternative forms of terms as the main entry (e.g., heterophilic antibody *vs*. heterophile antibody). In particular, many terms begin with immune or immuno- (e.g., immune elimination as part of the process of immunoediting). We have generally tried to use the form we find to be in most common usage, but if a desired entry is not found under one construction, it should be sought under the other.

Many definitions have been compiled from earlier sources, with or without modification, as indicated in the citation. When no citation is given, the term is newly defined. When a citation is given, the definition is more or less a quotation from the original. With the qualification "After", the general concept of the original has been retained with some rewording, often for consistency with IUPAC guidelines for glossaries. "Modified from" implies a concept specific to the source is retained but put into original wording. When a citation is indented following a *Note*, it refers only to the *Note*. The document has been put together with invaluable input from many colleagues and expert reviewers. Where flaws remain, they are the responsibility of the authors.

References

1. Duffus, J. H., Nordberg, M. and Templeton, D. M. (2007) Glossary of terms used in toxicology, 2nd ed. Pure Appl. Chem. **79**, 1153-1341.
2. Nordberg, M., Templeton, D. M., Andersen, O. and Duffus, J. H. (2009) Glossary of terms used in ecotoxicology. Pure Appl. Chem. **81**, 829-970.
3. Templeton, D. M. (2004) Mechanisms of immunosensitization to metals. Pure Appl. Chem. **76**, 1255-1268.
4. Klein, R., Schwenk, M., Heinrich-Ramm, R. and Templeton, D. M. (2004) Diagnostic

relevance of the lymphocyte transformation test for sensitization to beryllium and other metals. Pure Appl. Chem. **76**, 1269-1281.
5. Klein, R., Schwenk, M. and Templeton, D. M. (2006) Cytokine profiles in human exposure to metals. Pure Appl. Chem. **78**, 2155-2168
6. Schwenk, M., Klein, R. and Templeton, D. M. (2008) Lymphocyte subpopulations in human exposures to metals. Pure Appl. Chem. **80**, 1349-1364.
7. Schwenk, M., Klein, R. and Templeton, D. M. (2009) Immunological effects of mercury. Pure Appl. Chem. **81**, 153-167.

ACKNOWLEDGEMENTS

ALPHABETICAL ENTRIES

α:β T cell
Lymphocyte whose *T-cell receptor (TCR)* is a heterodimer of an α chain and a β chain.
Note: α:β T cells represent the majority of *thymocyte*s in the *thymus* and *T cell*s in the periphery.
See also *α:β T cell receptor*, *γ:δ T cell*.

α:β T cell receptor
T-cell receptor (TCR) consisting of a heterodimer of two different glycoprotein chains, designated α and β, assembled into an α:β heterodimer.

α-fetoprotein (AFP)
Serum protein, related to serum albumin in evolution, abundant in the fetus and reoccurring in the serum in liver cancer.
Note: it has various *immunomodulat*ing and *immunosuppressive* effects.

ABL oncogene
Gene resulting from a chromosomal translocation (9;22) that fuses sequences from the BCR gene with the ABL gene.
Note 1: This translocation creates the *Philadelphia chromosome*, found in most human patients with *chronic myelogenous leukemia (CML)*.
Note 2: The fusion protein encoded by BCR-ABL possesses unregulated *tyrosine kinase* activity.

ABO blood group system
System of *antigen*s expressed on *erythrocyte*s and used for typing human blood for *transfusion*.
Note: Individuals who do not express A or B antigens on their erythrocytes naturally form *antibodies* against them.
See also *blood group*.

abzyme
Antibody or antibody construct with catalytic activity.

accessory cell
Cell that assists in the *adaptive immune response* but does not directly mediate specific *antigen* recognition.
Note 1: Such cells include *phagocyte*s, *mast cell*s, *dendritic cell*s, and *NK cell*s.
Note 2: The term is often used to describe *antigen-presenting cell*s *(APC)*.

accessory molecule
Molecule other than *immunoglobulin (Ig)*, *T-cell receptor (TCR)*, or *major histocompatibility complex (MHC) molecule* that participates in *T lymphocyte* recognition and response to *antigen*.

acquired immunity
State of protection against pathogen-induced injury, with rapid *immune elimination* of pathogenic invaders owing to previous *immunization* or *vaccination*.
[1]

acquired immunodeficiency syndrome (AIDS)
Disease caused by infection with the *human immunodeficiency virus (HIV)*, assuming clinical relevance when an infected patient has lost most of his *CD4+ T cell*s, so that infections with opportunistic pathogens occur.

activation
See *lymphocyte activation*, *neutrophil activation*.

activation-induced cell death
Process by which *immune response*s end in the death of most of the responding *lymphocyte*s, leaving only a small number of resting *memory cell*s.
See also *apoptosis*.

active immunization
Immunization with *antigen*, as distinct from the transfer of *antibody* to an unimmunized individual, which is called *passive immunization*.

active systemic anaphylaxis (ASA) **test**
Test for determining whether a drug can cause *anaphylactic reaction*s in an animal following *immunization* with the drug.

acute lymphoblastic (lymphocytic) leukemia (ALL)
Highly aggressive, undifferentiated form of *lymphoid* malignancy derived from a progenitor cell that is thought to be able to give rise to both *T*- and *B-cell* lineages.
Note: Most of these *leukemia*s show partial differentiation toward the B-cell lineage (so called B-ALL) whereas a minority show features of T cells (T-ALL).
After [2]

acute myelogenous leukemia (AML)
Cancer characterized by rapid growth of abnormal *granulocyte*s that accumulate in the *bone marrow*.

acute phase protein
Serum protein, mostly produced in the liver, which rapidly changes in concentration (some acute phase proteins increase, some decrease) during the initiation of an *inflammatory response*.
[3]

acute-phase response (APR)
Physiological response stimulated by *cytokine*s including *interleukin*-1, interleukin-6, *interferon*s, and *tumor necrosis factor (TNF)*, characterized by increased vascular

permeability, fever, and increased levels of proteins (thus called *acute phase proteins*) such as *C-reactive protein (CRP)*, occurring within a few hours of initiation.

Note: Infection, *inflammation*, tissue injury, and occasionally neoplasms may trigger the APR.

acute rejection
Rejection of a tissue or organ *graft* from a genetically unrelated donor, typically occurring within 10-13 days of *transplantation*.
After [2]

acute respiratory distress syndrome (ARDS)
Acute lung failure characterized by alveolar and interstitial *edema*, perivascular pulmonary edema and hyaline membrane formation, resulting from a variety of underlying diseases that result in increased pulmonary vascular permeability.

adaptive immune response
Immune response based on the principle of clonal recognition, such that upon first exposure to an *antigen*, primed *lymphocytes* either differentiate into immune effector cells or form an expanded pool of *memory cells* that respond to secondary exposure to the same antigen by mounting an amplified and more rapid response.

Note: The response may be classified as cellular (*T cell*-mediated) or *humoral* (*antibody*-dependent).

adaptive immune system
Part of the *immune system* responsible for the *adaptive immune response.*

Addison disease (autoimmune)
Adrenocortical hypofunction characterized by hypotension, weight loss, anorexia, and weakness. The most common form is *idiopathic* Addison disease, mediated by *autoimmune* mechanisms. *Autoantibodies* specific to the adrenal cortex are specific diagnostic markers of this form.

Note: 21-Hydroxylase, a cytochrome P450 steroidogenic enzyme, is one of the major targets of adrenal autoantibodies in idiopathic Addison disease as well as in Addison disease in the context of autoimmune polyglandular syndromes (*polyendocrinopathies, autoimmune*). Hypofunction or failure of the adrenal gland may also be a manifestation of *antiphospholipid syndrome* due to thrombosis of the blood vessels of the adrenal glands.

After [1]

addressin
Extracellular protein of the venular *endothelium* serving as a *ligand* to a *homing receptor* for *lymphocyte*s.

Note: Addressins are glycoproteins recognized by *L-selectin*.

adenosine deaminase (ADA) deficiency

Lack of the enzyme adenosine deaminase (ADA), which catalyzes the deamination of adenosine and deoxyadenosine to produce inosine and deoxyinosine, respectively. Affected individuals have a form of *severe combined immunodeficiency (SCID)*.

adhesion molecule
Molecule belonging mainly to the *immunoglobulin*s, *integrin superfamily* (e.g., LFA-1, ICAM-1) or *selectin*s, expressed on the cell membrane of various cells including those of the *immune system*. Interaction of adhesion molecules with each other as *receptor* and corresponding *ligand* facilitates cooperation (cross-talk) of cells, *signal transduction* and information transfer between cells.
After [4]

adjuvant
1. In pharmacology, a substance added to a drug to speed or increase the action of the main component.
2. In *immunology*, a substance (such as aluminum hydroxide) or a suspension in oil of a dead organism (such as fragments of killed Mycobacterium) that increases the response to an *antigen*.
After [5]

adjuvant arthritis
Experimental model of *immunopathology* with features of *rheumatoid arthritis (RA)*, induced in rats by injection with bacterial products, which may be used to study anti-inflammatory (see *inflammation*) therapies.

adoptive transfer
Transfer, by *transplantation* of *immunocompetent* cells, of the capacity to mount an *immune response*.

adult respiratory distress syndrome (ARDS)
See *acute respiratory distress syndrome (ARDS)*.

adverse drug reaction
Appreciably harmful or unpleasant reaction resulting from an intervention related to the administration of a pharmaceutical product.
After [6]

adverse effect
Change in biochemistry, physiology, growth, development, morphology, behavior, or lifespan of an organism that results in impairment of functional capacity, impairment of capacity to compensate for additional stress, or an increase in susceptibility to other environmental influences.
[5]

adverse immunostimulation
Referring to *antigen*-non-specific, inappropriate, or unintended activation of a

component of the *immune system*.

Note: The distinction from *pseudoallergy* is subtle.

aeroallergen
Any airborne particle, such as a pollen grain or spore, that triggers an *allergic* reaction in sensitive individuals.

affinity
intrinsic affinity
Strength of binding (affinity constant) between a *receptor* (e.g., one *antigen*-binding site on an *antibody*) and a *ligand* (e.g., *epitope* on an antigen).
See also *avidity*.
[3]

affinity chromatography
Use of immobilized *antibody* (or *antigen*) to select specific antigen (or antibody) from a mixture. The purified *ligand* is then released by disrupting the antibody–antigen interaction, e.g., by changing the pH.
[3]

affinity maturation
Increase in *antibody affinity* for an *antigen* observed as the *humoral immune response* progresses.

agammaglobulinemia
See *X-linked agammaglobulinemia*.

agglutination
Clumping of particles, such as *erythrocyte*s or bacteria, caused by bivalent binding of *antibodies* to *antigen*s on the surfaces of adjacent particles.

Note: When the particles are erythrocytes, the phenomenon is called hemagglutination.

See also *hemagglutinin*, *prozone effect*.

agranulocytosis
Failure of the *bone marrow* to make sufficient *granulocyte*s, especially *neutrophil*s.

Note: This is normally identified by a *neutrophil* count $<0.5 \times 10^9$/L of blood.

allele
One of several alternate forms of a gene that occur at the same relative position (locus) on homologous chromosomes and which become separated during meiosis and can be recombined following fusion of gametes.
[5]

allelic exclusion
Phenomenon whereby, following successful rearrangement of one *allele* of an *antigen*

receptor gene, rearrangement of the other parental allele is suppressed, thereby ensuring each *lymphocyte* expresses only a single specificity of antigen receptor.

Note: This does not occur for α chains in *T lymphocyte*s.

allergen

Immunostimulant (see *immunostimulation*) *antigenic* substance that may or may not cause a clinically significant effect but which is capable of producing an immune reaction, often *immediate-type hypersensitivity*.

After [5]

See also *contact allergen*.

allergic

Immunologically hypersensitive.

See also *hypersensitivity*.

allergy

Symptoms or signs occurring in sensitized individuals (see *sensitization*) following exposure to a previously encountered substance (*allergen*) that would otherwise not cause such symptoms or signs in non-sensitized individuals. The most common forms of allergy are *rhinitis*, *urticaria*, *asthma*, and *contact dermatitis*.

Note: Except in the case of *contact allergen*s, it is often an *immunoglobulin E (IgE)-mediated hypersensitivity*, e.g., asthma, *eczema*, *hay fever* or food allergy.

alloantibody

Antibody produced against an *antigen* from another member of the same species.

See also *alloantigen*.

alloantigen

Antigen, present in some but not all individuals of a particular species, that arises from polymorphisms at the *major histocompatibility complex (MHC)* loci and stimulates intense reactions to *allograft* tissues from other individuals of the same species that do not produce it.

Note: The human *ABO blood group* system antigens and *Rhesus (Rh) factor* are important examples of alloantigens.

allogeneic

allogenic

Adjective applied to individuals of the same species that are genetically different.

Note: In *immunotoxicology* this generally refers to the use of genetically dissimilar cells to elicit a *cell-mediated immune response* in in vitro assays.

allograft

Tissue or organ *graft* between *allogeneic* individuals.

[3]

allotype

Allelic variant of an *antigen* that, because it is not present in all individuals, may be *immunogenic* in members of the same species that have a different version of the *allele*.
[3]

alloreactivity
Reactivity of an *antibody* with an *alloantigen*.

alopecia
Loss of hair, often associated with *autoimmune disease* [e.g., autoimmune thyroid diseases, *pernicious anemia*, *Addison disease*, *diabetes mellitus type 1*, or *systemic lupus erythematosus (SLE)*].
After [1]

alternative pathway (of complement activation)
Activation pathway involving *complement* components C3, Factor B, Factor D and *properdin* that, in the presence of a stabilizing activator surface such as microbial polysaccharide, generates the alternative pathway C3 convertase C3bBb.
[3]
See also *classical pathway (of complement activation)*.

alveolar macrophage
Macrophage found in the lung alveoli; it may remove and sometimes retain inhaled particulate matter.

alveolitis
1. Inflammation of alveoli.
2. Inflammation of a tooth socket.

alveolitis, exogen allergic
See *atypical interstitial pneumonia.*

amyloid
Fibrous protein secreted into the extracellular space where it forms amorphous deposits in multiple organs in some pathological states.
Note: Amyloid beta (Aβ) is found in neuronal plaques in the brain in Alzheimer disease.

anamnestic
Literally, "does not forget". Describing *immunological memory* giving rise to a rapid increase in *immunological response* after reexposure to *antigen*.
After [7]

anaphylactic shock
Immediate overreaction of the *immune system* to a drug or other agent in an individual who has previously encountered the agent and has produced *antibodies* to that agent.
Note: The major manifestation of anaphylactic shock is *angioedema*, which leads

to hypovalemia, obstruction of the airway, and bronchospasm; these in turn may lead to coma or death.

See also *anaphylaxis*.

anaphylactoid

Of or resembling *anaphylaxis*.

anaphylatoxin

Complement-derived protein fragment (e.g., C3a, C4a or C5a) capable of directly triggering *mast cell degranulation*, *chemotaxis*, smooth muscle contraction, and *inflammation*.

anaphylaxis

Life-threatening *type I hypersensitivity allergic reaction* (see *allergy*) occurring in a person or animal exposed to an *antigen* or *hapten* to which they have previously been sensitized.

Note: Consequences of the reaction may include *angioedema*, vascular collapse, shock (see *anaphylactic shock*), and respiratory distress.

[5]

ANCA-associated vasculitis

See *antineutrophil cytoplasmic autoantibody-associated vasculitis*.

anemia

Decrease in the number of *erythrocyte*s or total hemoglobin in the blood that results in a decrease in the oxygen-carrying capacity of the blood.

anergy

Lack of an *immune response*, usually taken as lack of response to common *recall antigen*s.

Note: The failure of *B* or *T cell*s to proliferate in response to defined *autoantigens* (*clonal anergy*) is a primary mechanism of *self-tolerance*.

After [1]

angioedema

angioneurotic edema

Swelling that occurs in the tissue just below the surface of the skin, most often around the lips and eyes, the mucous membranes and occasionally the viscera. It may be genetic, when it is referred to as hereditary angioedema (HAE), but is more usually caused by an *allergic* reaction to either food or medication, and is then called acquired angioedema (AAE).

Note 1: Angioedema may take from minutes to hours to develop. Severe angioedema can compromise the airway, and can be life threatening.

Note 2: Angioedema is often associated with dermatographism, *urticaria*, *erythema*, and *purpura*. It may sometimes be a sign of a condition such as *leukemia* or *Hodgkin disease*.

Note 3: Angioedema is similar to *hives*, but hives involve itchy red welts on the surface of the skin, whereas angioedema is a deeper swelling under the skin.

ankylosing spondylitis
Chronic inflammatory disease affecting the spine, sacroiliac joints, and large peripheral joints, having a major genetic predisposition.
After [7]

antibody
Protein [*immunoglobulin (Ig)*] produced by the *immune system* in response to exposure to an *antigenic* molecule and characterized by its specific binding to a site on that molecule (*antigenic determinant* or *epitope*).
[5]

antibody, therapeutic
Antibody administered with the aim of treating a disease.

antibody-dependent cellular cytotoxicity (ADCC)
antibody-dependent cell-mediated cytotoxicity
Cytotoxic reaction in which an *antibody*-coated *target cell* is directly killed by an *Fc receptor*-bearing *leukocyte*, e.g., *NK cell*, *macrophage*, *neutrophil*, or *eosinophil*.
After [3]

antibody-forming cell (AFC) **assay**
hemolytic plaque assay
Jerne plaque assay
plaque-forming cell (PFC) assay
Assay that measures the humoral immune response mediated by the concerted actions of *antigen-presenting cells*, *T lymphocyte*s, and *B lymphocytes*, generally by determination of murine primary *IgM* or *IgG* antibodies directed against the T cell–dependent sheep red blood cell (SRBC) surface antigens after in vivo sensitization.

Note: Due to involvement of multiple cell populations in mounting an antibody response, the AFC assay actually evaluates several immune parameters simultaneously. It is considered to be one of the most sensitive indicator systems for *immunotoxicology* studies.

[8]

antibody therapy
Use of an *antibody* to target specific cells (often tumor cells) or *signal transduction* pathways (often via *chemokine*s / *cytokine*s) in the treatment of disease.

Note: The main objectives are stimulation of the patient's *immune system* to attack malignant tumor cells and the prevention of tumor growth by blockage of specific cell *receptor*s.

anticoagulant, lupus

antibody, lupus
Autoantibody that binds to phospholipids and (or) proteins of the cell membrane in *systemic lupus erythematosus (SLE)*, and can interfere with blood clotting and tests of clotting function.

anti-DNA antibody
Antibody directed against single stranded or double stranded DNA.
See also *antinuclear antibody (ANA)*, *systemic lupus erythematosus (SLE)*.

anti-erythrocyte antibody
Antibody against molecules of the red blood cell, usually against membrane proteins, causing lysis of the red blood cells.
Note: Maternal *IgG* antibodies specific for the *Rhesus (Rh) factor blood group antigen* expressed against the *erythrocyte*s of the fetus may lead to hemolytic disease of the newborn.
See also *hemolytic anemia*.

antigen
Substance or a structural part (*epitope*) of a substance that is recognized by an *antibody*.
Note: It often causes the *immune system* to produce a specific *antibody* or specific cells and combines with a specific binding site (*paratope*) on the antibody or cells.
After [5]

antigen-binding groove
See *antigen-presenting groove*.

antigenic
Capable of stimulating *lymphocyte*s to produce *antibodies*.

antigenic determinant
Single *antigenic* site (*epitope*) usually exposed on the surface of a complex *antigen*.
[4]

antigenicity
Ability of an *antigen* to bind to a specific *antibody or T-cell receptor (TCR*); often a measure of its ability to produce *immunity*.

antigen presentation
Display of *antigen* as peptide fragments bound to *major histocompatibility complex (MHC) molecule*s on the surface of a cell.
*Note: T cell*s recognize antigen only when it is presented in this way.
[7]

antigen-presenting cell (APC)

Cell, such as a *dendritic cell* or *macrophage*, that is responsible for making *antigen*s accessible to *lymphocyte*s and other immune effector and regulatory cells making possible specific recognition by *receptor*s on the cell surface.

Note: In a more restricted way, used to describe *major histocompatibility complex (MHC) class II*-positive cells (*accessory cells*) that internalise and degrade an antigen (generally by *phagocytosis*), before a fragment of the antigen molecule is presented on the APC cell surface in association with an *major histocompatibility complex (MHC) molecule*. This complex is recognized by either *B cell*s via surface-bound *immunoglobulin (Ig)* molecules, or by *T cell*s via the *T-cell receptor (TCR)* for the antigen. Induction of a specific *immune response* then proceeds.

antigen-presenting groove

1. Pocket in a *major histocompatibility complex (MHC) molecule* that binds *antigen* for *antigen presentation*.
2. Hydrophobic binding region in the CD1 protein that anchors lipid-containing antigens causing exposure of the peptide or carbohydrate moiety in a position enabling *T cell receptor (TCR)* contact.

antigen processing

Cleavage of protein *antigen*s in *antigen-presenting cells (APC)*.

Note: The *immunogenic* peptides interact with the binding sites of *MHC class II* products (exogenous antigens) or with those in *MHC class I* products (endogenous antigens, including viruses). The processed antigen-MHC complex is recognized by the *antigen receptor* complex of *T lymphocyte*s.

Modified from [4]

See also *antigen presentation*.

antigen receptor

Specific *antigen*-binding *receptor* on *T* or *B lymphocyte*s that is transcribed and translated following rearrangements and translocation of *V*, *D*, and *J gene*s.

After [7]

antigen recognition

Ability of highly specialized proteins of the *immune system* to recognize *antigen*s and specifically bind to them.

Note: Types of antigen recognition include that by *antibodies*, *T-cell receptor*s *(TCR)*, and *Toll-like receptor*s *(TLR)*.

anti-idiotypic antibody

Antibody raised against *antigenic determinant*s unique to the *variable region* of a single antibody.

[2]

See also *idiotope*, *idiotype*, *idiotypic network*.

anti-isotypic antibody

Antibody against universal features of a given *constant (C) region isotype* (such as γ or μ) of one species that is made by immunizing a member of another species with that isotype.

Note: Such antibodies will bind any antibody of that isotype, and are thus useful for detecting bound antibody molecules in *immunoassay*s and other applications.

[2]

antimitochondrial antibody (AMA)
Autoantibody producing a mitochondrial staining pattern on sections of various tissues and on tumor cell monolayers.

Note: According to the fluorescence pattern, different subtypes can be differentiated. Antimitochondrial antibodies of the subtype 2 (AMA-M2) are directed against *antigen*s of three related 2-oxo acid dehydrogenase complexes (e.g., the E2 subunit of the pyruvate dehydrogenase complex, PDC-E2) localized to the inner mitochondrial membrane. AMA-M2 is a specific marker of *primary biliary cirrhosis (PBC)*.

After [1]

antineutrophil cytoplasmic autoantibody (ANCA)
Antibody against *antigen*s in the cytoplasm of *neutrophil*s.
See *antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis*.

antineutrophil cytoplasmic autoantibody (ANCA)**-associated vasculitis**
One of a group of *autoimmune systemic* vasculitides associated with *antineutrophil cytoplasmic autoantibodies (ANCA)*, e.g., *Wegener granulomatosis (WG)*, *microscopic polyangiitis*, and Churg-Strauss syndrome.
[1]

antinuclear antibody (ANA)
antinuclear factor (ANF)
Antibody, detectable in the blood, that has the capability of binding to a substance, e.g., DNA, within the nucleus of the cells.

Note: ANAs are found in patients whose *immune system* may be predisposed to cause *inflammation* against their own body tissues. ANAs indicate the possible presence of *autoimmunity* and are an indication of *autoimmune disease*, such as *rheumatoid arthritis (RA)*, *scleroderma*, *Sjögren syndrome*, *systemic lupus erythematosus (SLE)*, and *mixed connective tissue disease (MCTD).*

Modified from [4]

antiphospholipid syndrome (APS)
One of the most common *autoimmune disease*s, characterized by thrombosis, recurrent spontaneous abortions, and the presence of antiphospholipid *antibodies*.

Note: Antiphospholipid syndrome may occur as an isolated disease (primary APS) or in combination with another autoimmune disease, especially *systemic*

lupus erythematosus (SLE) (secondary APS).
[1]

antiserum
The *blood serum* from an immune individual that contains *polyclonal antibodies* against the agent used for *immunization*.

anti-sheep red blood cell IgM response (SRBC) **assay**
Test to determine *T cell*-dependent *antibody* response, usually by *ELISA*. Sheep red blood cells (SRBC) are used as an *antigen*. Often referred to as the *plaque assay*.
Note: A similar test is often performed with the *tetanus toxoid* as the antigen.

antitoxin
Antibody specific for *exotoxin*s produced by certain microorganisms such as the causative agents of diphtheria and tetanus.
[7]

APECED syndrome
See *polyendocrinopathy, autoimmune*.

aplastic anemia
Greatly decreased formation of *erythrocyte*s and hemoglobin, usually associated with pronounced *granulocytopenia* and *thrombocytopenia*, as a result of hypoplastic or aplastic *bone marrow*.
[9]
Note: The diagnosis requires *bone marrow* biopsy to demonstrate replacement of blood cell precursors with fat cells and rule out other causes of *pancytopenia* such as neoplastic infiltration.

apopto/**sis** (n), /**tic** (adj)
Active process of programmed cell death, requiring metabolic energy, often characterized by fragmentation of DNA and cell deletion without associated *inflammation*.
[5]

appendix
Lymphoid tissue located at the beginning of the colon.
See also *gut-associated lymphoid tissue (GALT)*.
[7]

arthritis
Inflammation of a joint or joints.
See also *rheumatoid srthritis (RA)*.

Arthus reaction
Gell and Coombs Type III reaction

Local *antibody*-mediated *hypersensitivity* reaction in which *antigen*-antibody complexes which fix *complement* are deposited in the walls of small vessels, often in the skin, causing acute *inflammation* with an infiltration of *neutrophil*s.

asthma
Chronic respiratory disease characterized by bronchoconstriction, excessive mucus secretion, and edema of the pulmonary alveoli, resulting in difficulty in exhaling, wheezing, and cough.
[5]

ataxia telangiectasia (AT)
Disease characterized by staggering gait, multiple disorganized blood vessels, and an *immunodeficiency*, associated with a protein called ataxia telangiectasia-mutated (ATM), a protein kinase thought to be important in detection of double-stranded DNA breaks.
After [7]

atopic allergy
Immunoglobulin E (IgE)-mediated hypersensitivity, including *asthma*, *eczema*, *hay fever* and food allergy.
After [3]
See also *atopy*.

atopic dermatitis
Inflammation of the skin in *atopic* individuals.
Note: The term is broader than *atopic eczema*.
After [4]

atopic eczema
Chronic skin disease, often localized on flexural surfaces, in individuals with propensity to develop *immunoglobulin E (IgE)*-mediated *allergy*.
Note: The term describes *eczema* occurring in *atopic* individuals and does not imply mechanisms.
After [4]

atop/**y** (n), /**ic** (adj)
Of, relating to, or caused by a hereditary predisposition toward developing certain *hypersensitivity* reactions, such as *hay fever*, *asthma*, or chronic *urticaria*, upon exposure to specific *antigens*.

attenuated vaccine
Vaccine made from a live organism that targets cells of the *immune system* but has been engineered or weakened so as not to cause disease.
See also *inactivated vaccine*, *live attenuated vaccine*.

atypical interstitial pneumonia

Acute or chronic respiratory distress in cattle, in the absence of toxemia or other *systemic* signs that are characteristic of other pneumonias.

Note 1: The causes are unknown, but may include *allergic* reactions or toxicity due to conversion of *tryptophan* to toxic 3-methyl indole by gut flora.

Note 2: Also called bovine pulmonary emphysema, enzootic bovine adenomatosis, pulmonary adenomatosis, mold *hypersensitivity*, fog fever, and panters.

autoantibody
Immunoglobulin (Ig) antibody that is directed against the organism's own *antigen*(s).
After [1]

autoantigen
Antigenic component of an individual's tissues which may be a target of *autoimmune* responses by autoreactive *B cell*s (*autoantibodie*s) or *T cell*s, including proteins (e.g., enzymes, structural proteins), glycoproteins (e.g., 2-glycoprotein I), nucleic acids, (e.g., double-stranded DNA), phospholipids (e.g., *cardiolipin*), and glycosphingolipids (e.g., gangliosides).
See also *self-tolerance.*
After [1]

autochthonous
Pertaining to self.

autocrine
Type of signaling in which a cell secretes a chemical messenger that binds to *receptor*s on the same cell, leading to changes in the cell.
See also *paracrine*.

autograft
Tissue transplant (see *transplantation*) from one site to another in an individual.
After [7]

autoimmune
Of or relating to an *immune response* by the body against one of its own cells or tissues.

autoimmune disease
Pathological condition resulting when an organism produces *antibodies* or specific cells that bind to constituents of its own tissues (*autoantigen*s) and cause tissue injury. Examples of such disease may include *rheumatoid arthritis (RA)*, *myasthenia gravis*, *systemic lupus erythematosus (SLE)*, and *scleroderma*.
[5]

autoimmune hemolytic anemia
Autoimmune disease in which *antibodies* initiate *complement* lysis of *erythrocyte*s.

Note: Autoimmune hemolytic anemia may be *idiopathic*, secondary to

lymphoproliferative, autoimmune [e.g., *systemic lupus erythematosus (SLE)*], or chronic inflammatory disorders, postinfectious or drug-induced.
Modified from [1]

autoimmune hepatitis (AIH)
Chronic *autoimmune*-mediated hepatic *inflammation* usually characterized by *antinuclear (ANA)*, smooth muscle (SMA)/anti-F-actin, *liver-kidney microsomal (LKM)*, and (or) soluble liver antigen (SLA) antibodies.
After [1]

autoimmune lymphoproliferative syndrome (ALPS)
Canale-Smith syndrome
Disease characterized by *lymphadenopathy*, hepatosplenomegaly, *autoimmune cytopenia*s, and *hypergammaglobulinemia*.
After [1]

autoimmune polyendocrine syndrome (APS) **type 1 or 2**
Heterogeneous group of rare diseases characterised by *autoimmune* activity against more than one endocrine organ, although non-endocrine organs can also be affected.

Note 1: Autoimmune polyendocrine syndrome, type 1 is known as the *candidiasis*-hypoparathyroidism-*Addison disease* syndrome after its main features:
a) A mild immune deficiency, leading to persistent *mucosa*l and cutaneous infections with Candida yeasts. There is also decreased function of the *spleen* (asplenism).
b) Autoimmune dysfunction of the parathyroid gland (leading to hypocalcemia) and the adrenal gland (Addison disease).

Note 2: Autoimmune polyendocrine syndrome, type 2 (also known as Schmidt syndrome) is more heterogeneous, occurs more often and has not been linked to one gene. Features of this syndrome are Addison disease, hypothyroidism (*Hashimoto thyroiditis*), and *diabetes mellitus type 1*. Patients are at a higher risk when they carry a particular *human leukocyte antigen (HLA)* genotype (e.g., DQ2, DQ8 and DRB1*0404).

autoimmune regulator (AIRE)
DNA-binding protein involved in immunoregulation (probably in the establishment and maintenance of *tolerance*).
[1]

autoimmunity
Immune response to "self" tissues or components.

Note: Such an immune response may have pathological consequences leading to *autoimmune diseases*.

See also *autoantigen*, *self-antigen*.

autoinflammatory disease

Unregulated *inflammation* without significant levels of *autoantibodies* or autoactivated *T cell*s, or evidence of infection, but rather caused by genetic disturbance of the mechanisms that initiate and control inflammation.

autologous
From the same individual.

autologous antibody
Antibody derived from a specific individual, acting within that individual.
See also *heterologous antibody*.

autophag/y (n) /**ic** (adj)
Digestion and breakdown in *lysosome*s of a cell's own proteins and (or) organelles.
Note: It may be one route by which proteins can be processed for *antigen presentation*.
See also *heterophagy*, *macroautophagy, microautophagy*, *mitophagy, pexophagy*.

autoreactivity
Immune response directed at *self-antigen*s.

avidity
functional affinity
Binding strength between two molecules (e.g., *antibody* and *antigen*) taking into account the valency of the interaction. Thus the avidity will always be equal to or greater than the *affinity*.
[3]

β_2-microglobulin
Small (12 kDa) protein forming part of the structure of *major histocompatibility complex (MHC) class I*-encoded molecules.
Note: The presence of β_2-microglobulin in urine is a common indicator of renal tubular dysfunction.

B-1/B-2 cells
B-1/B-2 lymphocytes
Two major subpopulations of *B lymphocyte*s.
Note 1: The majority of *B cell*s are B-2 which express low levels of surface IgM, higher levels of surface IgD, do not express CD5, and are CD43 -, *CD23* + ; they are directly generated from precursors in the *bone marrow*, and secrete highly specific antibody.
Note 2: B-1 cells bear high levels of surface *immunoglobulin M (IgM)*, show lower levels of surface *immunoglobulin D (IgD)*, are CD43 +/*CD23* -, and most express the cell surface *antigen* CD5. They are self-renewing, and frequently secrete high levels of *antibody* that binds to a range of antigens ('polyspecificity') with a relatively low *affinity*.
After [3]

B7 molecule
Costimulatory molecule (see *costimulation*) on the surface of *T cell*-activating *antigen-presenting cell*s *(APC)*, allowing full *activation* of T cells that are bound to *major histocompatibility complex (MHC*)-peptide complexes.

Note: Whereas binding of B7 molecules to CD28 is stimulatory, binding to *cytotoxic T-lymphocyte antigen-4 (CTLA-4)* decreases T cell activity and participates in *tolerance*.

B cell
See *B lymphocyte*.

B-cell linker protein (BLNK)
Adaptor protein operating in *B cell*s that, upon phosphorylation, recruits signaling molecules to membrane *lipid raft*s.

B-cell stimulatory factor (BSF)
Generic name given to *B cell*-specific growth and differentiation factors involved in the *T cell*-dependent *activation* of B cells. Many are now identified as specific *interleukin*s *(IL).*

B-cell receptor (BCR)
Receptor on the surface of a *B cell* consisting of transmembrane *immunoglobulin (Ig)* that recognizes a specific *antigen*.

B lymphocyte
B cell
Bone marrow-derived *lymphocyte*, expressing an *antigen-receptor* complex composed of membrane-bound *immunoglobulin (Ig)* and associated molecular chains.

*Note: B-cell receptor*s *(BCR)* interact with *epitope*s directly [no *major histocompatibility complex (MHC) restriction*]. Mature activated B lymphocytes (*plasma cell*s) produce *antibody* and are efficient *antigen-presenting cell*s *(APC)*.

After [4]

B-lymphocyte chemokine (CXCL13)
Chemokine that attracts *B cell*s and activated *T cell*s into the follicles of peripheral *lymphoid tissue*s.
After [2]

B-lymphocyte-induced maturation protein 1 (BLIMP-1)
Transcriptional repressor in *B cell*s, that switches off genes required for B cell proliferation in the *germinal center*, and for *class switching* and *affinity maturation*.

Note: B cells in which BLIMP-1 is induced, become *plasma cell*s.
[2]

bacille Calmette–Guérin (BCG)
Attenuated Mycobacterium tuberculosis used both as a specific *vaccine* for tuberculosis and as an *adjuvant*.
[3]

Note: Also used as an *immunostimulant* in cancer therapy (e.g., in bladder cancer).

BALB/c mouse
Inbred albino mouse strain, substrains of which produce *plasmacytoma*s on injection with mineral oil, useful for the production of *monoclonal antibodies*.

bare lymphocyte syndrome (BLS)
Rare, recessive genetic condition in which the products of one or more genes required to switch on *major histocompatibility complex (MHC) class I* or *MHC class II* genes are defective or absent. As a consequence, MHC class I (BLS1) or MHC class II (BLS2) genes are not expressed, leading to severe *immunodeficiency*.

basophil
Type of *granulocyte* found in the blood and resembling the tissue *mast cell*.
[3]

basophilic degranulation
Loss of granules in basophilic cells (see *basophil*), associated with the release of active substances from the cells, characteristic of *type I immediate hypersensitivity*.

Bcl-2
Member of the Bcl protein family that protects cells from *apoptosis* by binding to the mitochondrial membrane.

Note: It is encoded by the bcl-2 gene, which was discovered at the breakpoint of an oncogenic chromosomal translocation in *B-cell leukemia*.

After [2]

BCR-ABL
See *ABL oncogene*.

Behcet disease
Chronic *vasculitis* of unknown origin, characterized by ulcerations and skin rash and treated by *immunosuppression*.

Bence-Jones protein
Excess circulating *kappa (κ)-light chain* found in the urine of patients with *multiple myeloma*.

benign monoclonal gammopathy
Nonmalignant overproduction of *γ globulin* by a single *clone* of *lymphocyte*s.

biolistics

Use of small particles, e.g., colloidal gold, as a vehicle for carrying agents (drugs, nucleic acid, etc.) into a cell.

Note: Following coating with the desired agent(s), the particles are fired into the dermis of the recipient using a helium-powered gun.

[3]

biopanning
Technique for selection of peptides with high *affinity* binding to a chosen target.

bispecific antibody
Artificially produced hybrid *antibody* in which each of the two *antigen*-binding arms is specific for a different antigenic *epitope*. Such antibodies, which can be produced either by chemical cross-linkage or by recombinant DNA techniques, can be used to link together two different antigens or cells, e.g., a *cytotoxic T lymphocyte* and a tumor cell.
[3]

blast
Immature stage in cell development, before the appearance of the definitive characteristics of the cell; used also as a word termination, as in erythroblast, etc.

blastogenesis assay
See *lymphocyte transformation test (LTT)*.

Blau syndrome
Rare familial inflammatory disease characterized by *arthritis*, *dermatitis* and uveitis.

blocking antibody
Antibody that prevents other antibodies from combining with a specific *antigen* but does not itself produce an *immunological response* when combined with that antigen.

blood-brain barrier
Physiological interface between brain tissues and circulating blood created by a mechanism that alters the permeability of brain capillaries, so that some substances are prevented from entering brain tissue, while other substances are allowed to enter freely.

Note: The blood-brain barrier normally keeps cells of the *immune system* outside the brain.

After [5]

blood dyscrasia
Presence of abnormal material in the blood, usually applied to diseases affecting blood cells or *platelet*s.
[9]

blood group
blood type
Any of the various types of blood whose characteristic *erythrocyte* surface *antigen*s

determine compatibility in *transfusion*.
See also *ABO blood group*.

blood group antigen
Surface *antigen* on *erythrocyte*s, detectable with a specific *antibody* from other individuals.

Note: The major blood group antigens ABO and Rh (Rhesus) are used in routine blood banking to type blood, but there are many other blood group antigens that can also be detected in *cross-matching*.

See also *ABO blood group system*, *blood group*, *Rhesus (Rh) factor*.

blood-placenta barrier
Physiological interface between maternal and fetal blood circulations that filters out some substances that could harm the fetus while favoring the passage of others such as nutrients.

Note 1: Many fat-soluble substances such as alcohol are not filtered out, and several types of virus can also cross this barrier.

Note 2: The effectiveness of the interface as a barrier varies with species and different forms of placentation.

Note 3: Immunoglobulin G (IgG) antibodies are specifically transported across the barrier and reach the same levels in the newborn, as in the mother.

After [5]

blood plasma
See *plasma*.

blood serum
See *serum*.

Bloom syndrome
Disease caused by mutations in a DNA helicase and characterized by low *T cell* numbers, reduced *antibody* levels, and an increased susceptibility to respiratory infections, cancer, and radiation damage.
After [2]

bone marrow
See *marrow, bone*.

bone marrow transplantation
Transfer of *bone marrow* from a donor to a recipient whose bone marrow has been ablated.

Note 1: Bone marrow transplantation is used to treat both non-neoplastic and neoplastic conditions not amenable to other forms of therapy.

Note 2: It has been used especially in cases of *aplastic anemia*, *acute lymphoblastic (lymphocytic) leukemia (ALL)*, and *acute myelogenous leukemia* (AML).

booster
Portion of an immunizing agent (see *immunization*) given at a later time to stimulate the effects of a previous dose of the same agent.

bradykinin
Vasoactive peptide and inflammatory mediator (see *inflammation*) produced at sites of tissue damage.

bronchus-associated lymphoid tissue (BALT)
See *mucosa-associated lymphoid tissue (MALT)*.

bronchial provocation test
Test of alteration of lung function induced by inhalation of an *allergen* or airway-constricting agent, providing information on bronchial responsiveness.

Bruton agammaglobulinemia
See *X-linked agammaglobulinemia*.

Buehler assay (BA)
Buehler test
Skin sensitization test for *contact allergic dermatitis* in which a test substance is applied to the shaved flank of a Guinea pig in an occlusive patch for 6 h at 0, 1, and 2 weeks, followed by *challenge* of the untreated flank at 4 weeks.

bullous skin disease, autoimmune
Any of several *autoimmune disease*s characterized by intraepidermal or subepidermal blisters (e.g., *pemphigus vulgaris*, bullous pemphigoid) and highly specific *autoantibodies* against components of the desmosome or hemidesmosome (e.g., desmoglein 3, BP180).
After [1]

Burkitt lymphoma
Lymphoma caused by *Epstein-Barr virus (EBV)*, occurring mainly in sub-Saharan Africa.

bursa of Fabricius
Primary *lymphoid* organ in avian species, located at the cloacal-hind gut junction; it is the site of *B cell maturation*.
[3]

bystander effect (in immunology)
Positive or negative effect on the *immune system* seen after exposure to certain drugs, radiation, and other agents, induced by non-immune mechanisms.
See also *bystander suppression*.

bystander suppression

Suppression of an *immune response* to an *antigen* due to *tolerance* to an unrelated (hence bystander) antigen.
See also *bystander effect*.

C1 esterase inhibitor
See *C1 inhibitor*.

C1 inhibitor
C1 esterase inhibitor
Plasma glycoprotein secreted primarily by the liver and acting as a serine proteinase inhibitor (serpin), inhibiting C1 components of the *complement system*.
Note 1: It also inhibits coagulation factors XI and XII and *kallikrein*.
Note 2: Patients with C1 inhibitor deficiency may manifest *systemic lupus erythematosus (SLE)*, *glomerulonephritis*, or pyogenic infections.
See also *hereditary angioneurotic edema*.

CC chemokine
See *chemokine*.

CD1
Cell surface protein of *antigen-presenting cells (APC)* involved in presentation of lipopeptide or glycolipid *antigen*s.
See also *antigen-presenting groove*.

CD3
Molecule composed of five polypeptide chains associated with the heterodimer *T-cell receptor (TCR)*, forming the T-cell receptor complex (TCR/CD3); CD3 transduces the activating signals when *antigen* binds to the TCR.
[1]

CD4
Cell surface *antigen* belonging to the *immunoglobulin (Ig) superfamily* of molecules and a marker of *T helper cell*s.
Note: As an adhesion molecule, it interacts with the non-polymorphic part of *major histocompatibility complex (MHC) class II gene product*.
[1]

CD4+/CD25+ T cell
Subtype of *CD4+ regulatory T cell (Treg)* with potential role in the regulation of *immune* homeostasis.
Note 1: These cells seem to be important in preventing the development of *autoimmune disease*s (depletion leads to the spontaneous development of various autoimmune diseases in genetically susceptible animals; transfer prevents the development of organ-specific *autoimmunity*).
After [1]
Note 2: Activated (see *activation*) *T cell*s may also have this phenotype. Treg cells

may be further distinguished by positivity for a protein marker *Foxp3*.

CD5+ B lymphocyte
Lymphocyte of type B-1a, which is predominant in fetal *lymphoid* organs and in *neonatal* cord blood.

Note 1: In adults, these cells range from 2% to 6% of total mononuclear cells in peripheral blood. They utilize an *immunoglobulin (Ig) variable (V) gene* repertoire different from that of CD5**-** *B cell*s and they produce *natural autoantibodies*.

Note 2: The expansion of autoreactive B1-a cells has been reported in peripheral blood of patients with autoimmune diseases [e.g., *rheumatoid arthritis (RA)*, *Sjögren syndrome*, *antiphospholipid syndrome (APS)*]. In RA these cells can account for up to 60% of circulating B cells and may produce *rheumatoid factor*.

After [1]

CD8
Cell surface molecule belonging to the *immunoglobulin (Ig) superfamily* of molecules found, among others, on *cytotoxic T cell*s, which binds to *major histocompatibility complex (MHC) class I molecule*s.
After [1]

CD8+ T suppressor cell
Outdated term for CD8+ *cytotoxic T lymphocyte* (CTL, Tc) The term "*suppressor T cell*" is nowadays reserved for *regulatory T cell (Treg)*.

CD16
Low-*affinity Fc-γ receptor* (Fc-γ-RIII) expressed mainly on *natural killer (NK) cells*, *granulocyte*s and *macrophage*s, mediating *antibody-dependent cellular cytotoxicity (ADCC)*.
[4]

CD23
Low-*affinity Fc-ε receptor* induced by *interleukin*-4 (IL-4) and expressed on activated *B cell*s (see *lymphocyte activation*) and *macrophage*s.
[4]

CD25
α-chain of the *interleukin*-2 (IL-2) receptor.
[1]

CD40 ligand (CD40L)
Essential molecule for normal switching signaling through binding to CD40 on *B cell*s. The interaction of CD40L and CD40 is also critical for optimal *T cell* function. See *hyper immunoglobulin M (IgM) syndrome*.
[1]

CD45
See *leukocyte common antigen (LCA)*.

C domain
See *constant (C) region*.

C gene
See *constant (C) gene*.

C-reactive protein (CRP)
Serum protein produced by liver cells as part of the *acute-phase response*, which acts as a stimulus of the *classical pathway of complement activation*.

Note: CRP binds to the phosphorylcholine component of the C-polysaccharide, a component of the surface of many bacteria and fungi, resulting in *opsonization* for enhanced *phagocytosis*.

C region
See *constant (C) region*.

C-type lectin
Any of a large family of Ca^{2+}-dependent *lectin*s; members of this family share primary structural homology in their carbohydrate-recognition domains and include many endocytic *receptor*s, many proteoglycans, and all known *collectin*s and *selectin*s.

Note: The C-type lectins are involved in many *immune system* functions, such as *inflammation* and *immunity* to tumor and virally infected cells, whereas the *collectin*s are involved in *innate immunity*.

After [10]

CXC chemokine
See *chemokine*.

CX_3C chemokine
See *chemokine*.

cadherin
Calcium-dependent, transmembrane glycoprotein occurring in cell-cell contacts (desmosomes) and functioning as an *adhesion molecule*.

Note: Cadherins may mediate *lymphocyte homing* and are also important elements in cellular *signal transduction*.

calcineurin inhibitor
Any member of a group of immunomodulating (see *immunomodulation*) drugs that bind to the cytosolic protein cyclophilin of *T lymphocyte*s, thus inhibiting the phosphatase calcineurin, an inducer of *interleukin*-2 (IL-2) formation.

Note: Calcineurin inhibitors include potent immunomodulating drugs, such as

cyclosporin, tacrolimus, pimecrolimus, and voclosporin (see Annex II).

Canale-Smith syndrome
See *autoimmune lymphoproliferative syndrome (ALPS)*.

candidiasis
candidosis
moniliasis
Infection with a fungus of the genus Candida, especially C. albicans, that usually occurs in the skin and mucous membranes of the mouth, respiratory tract, or vagina but may invade the bloodstream, especially in *immunocompromised* individuals.
See also *thrush.*
[11]

capping
Active process whereby cross-linking of cell surface molecules (e.g., by *antibody*) leads to aggregation and subsequent migration of the molecules to one pole of the cell.
[3]

carcinoembryonic antigen (CEA)
Membrane glycoprotein *epitope* normally present in the fetal gastrointestinal tract and elevated in many patients with various carcinomas.
After [7]

cardiolipin
1,3-Bis(*sn*-3'-phosphatidyl)-*sn*-glycerol, the main target of antiphospholipid *antibodies*.
See also *antiphospholipid syndrome (APS)*.

carrier (in immunology)
Any molecule that, when conjugated to a non-*immunogen*ic molecule (e.g., a *hapten*), makes the latter immunogenic by providing *epitope*s for *helper T lymphocyte*s *(Th)* that the hapten lacks.
[3]

caspase
Any member of a family of intracellular cysteine proteinases that cleave proteins at specific aspartic acid residues to initiate or promote *apoptosis*.

caveola
Invagination on the cell surface (plasma membrane), enriched in caveolin proteins, cholesterol, and glycosphingolipids, important in various processes including *pinocytosis* and *signal transduction*. A type of *lipid raft*.

celiac disease
gluten enteropathy
non-tropical sprue

Autoimmune disorder occuring in genetically predisposed individuals, characterised by *immune intolerance* to the α-gliadin component of gluten, a protein found in wheat, barley, and rye. Resultant *inflammation* of the *mucosa* of the upper small intestine is associated with malabsorption of nutrients and a wasting illness follows from this.

cell-mediated cytotoxicity
Lysis of a *target cell* initiated by a *T-lymphocyte* binding to surface *antibodies* or *antigen*-bound *major histocompatibility complex molecule*s.

cell-mediated immune response
Specific *immune response* in which *T lymphocyte*s mediate the effects, either through the release of *cytokine*s or through *cytotoxicity*.
[4]

cell-mediated immunity (CMI)
Immune response mediated by *antigen*-specific *T lymphocyte*s, either through the release of *cytokine*s or through *cytotoxicity*, in contrast with *humoral immunity*, which is *antibody*-mediated.

Note: Cell-mediated immunity may be expressed as immune regulatory activity (primarily mediated by *CD4+ helper T lymphocyte*s *(Th)*, possibly important in preventing *autoimmune disease*s) or immune effector activity (mediated largely by *CD8+ cytotoxic T cell*s).

See also *immune regulation*.

cell-mediated response
See *cell-mediated immune response*.

cellular immunity
See *cell-mediated immunity (CMI)*.

central tolerance
Specific immunological *tolerance* due to the induction of *lymphocyte apoptosis* or *anergy* within the primary *lymphoid* organs (*bone marrow* in the case of *B cell* tolerance and the *thymus* for *T cell*s).
[3]

challenge (in immunology)
Induction or evaluation of an *immune response* in an organism by administration of a specific *antigen* to which it has been sensitized.

chaperone-mediated autophagy (CMA)
Type of *autophagy* targeting only those proteins that are recognized by the binding of an hsc70-containing chaperone / co-chaperone complex.

chemokine
Any of a large family of small proteins, produced by many types of cells, that attract and guide *lymphocyte*s to sites of infection and *inflammation* or to other sites, such as those

associated with lymphocyte development and with migration into *lymph node*s.

Note 1: Chemokines fall into two main categories: CC chemokines (β-chemokines) have two cysteine (C) residues near the amino terminus of the protein, whereas in CXC chemokines (α-chemokines) the two cysteines are separated by a single variable amino acid (X). There are two other groups of chemokines – C chemokines (γ- chemokines) that have two cysteines, one N-terminal cysteine and one cysteine downstream; and CX_3C chemokines (or δ-chemokines) that have three amino acids between the two cysteines.

Note 2: Chemokines act in conjunction with other factors, such as *tumor necrosis factor (TNF-α)*, to induce the *adhesion* factors that attach lymphocytes to the blood vessel wall before they move through it into the tissues.

chemotactic factor
Biologically active substance, such as a *chemokine* or *anaphylatoxin*, that induces a concentration gradient-dependent movement of cells.
See also *chemotaxis*.

chemotaxis
1. General**.** Movement of an organism or cell along a concentration gradient of a chemical.
2. In immunology. Movement of cells up a concentration gradient of a chemical attractant (*chemotactic factor*), such as a *chemokine* or other *cytokine*.
[3]

chemotype
chemovar
Character of a plant or microorganism based on a metabolite distinct from that found in other members of the same species.

chimeric
Composite of genetically distinct individuals, e.g., following an *allogeneic bone marrow graft*.
[3]

chloracne
Acne-like eruption caused by exposure to certain chlorinated organic substances such as polychlorinated biphenyls or 2,3,7,8-tetrachlorodibenzo-*p*-dioxin [2,3,7,8-tetrachlorooxanthrene] and other polychlorinated dibenzodioxins and furans.
[5]

Note: The lesions are most frequently found on the cheeks, behind the ears, in the armpits and groin region.

chromate uptake assay

Method used in *immunotoxicology* to quantify the toxic effect of a substance on *leukocyte*s by measuring uptake of ^{51}Cr-labeled chromate.

chromium release assay
^{51}Cr release assay
*Immunotoxici*ty assay that can be used to assess either *natural killer (NK) cell* or *cytotoxic T cell* activity or *macrophage* activity. When incubated with ^{51}Cr-labeled chicken red blood cells (cRBC), NK and cytotoxic T cells lyse the cRBC and thus induce the release of ^{51}Cr into the medium. In contrast, macrophages phagocytose cRBC, and are then lysed to assess the amount of ^{51}Cr they have taken up.

Note: The assay is usually applied to measure parameters of innate immunity.

See also *chromate uptake assay*.

chronic allergic inflammation
Disease of airways, skin, eyes and other organs, resulting from repeated or continuous exposure to an *allergen* and involving *immunoglobulin E (IgE)* formation, IgE-induced *histamine*-release from *mast cell*s, liberation of mediators such as *cytokine*s and *prostaglandin*s, and local *inflammation* characterized by infiltrating *leucocyte*s; it results in augmented susceptibility to the allergen.

chronic graft rejection
See *chronic rejection*.

chronic granulomatous disease
Immunodeficiency disease in which multiple *granuloma*s form as a result of defective elimination of bacteria by *phagocyte*s.

Note: It is caused by deficiency of the *NADPH oxidase* system of enzymes that generates superoxide involved in bacterial killing.

After [2]

chronic lymphocytic leukemia (CLL)
B cell tumor found in the blood.

Note: The great majority of these tumors express *CD5* and unmutated *variable (V) gene*s and are therefore thought to arise from *B-1 cell*s.

After [2]

chronic lymphocytic thyroiditis
See *Hashimoto thyroiditis*.

chronic myelogenous leukemia (CML)
Cancer characterized by overgrowth of the *bone marrow* with malignant white blood cells, usually exhibiting a chromosomal abnormality (Philadelphia chromosome), which causes uncontrolled proliferation of cells that are released into peripheral blood.

chronic rejection

Immunologically triggered reaction occurring in a transplanted organ or tissue, leading to progressive destruction and finally failure of the transplanted organ occurring two months to many years after *transplantation*.

Note: In contrast, hyperacute rejection caused by preformed *antibodies* starts within minutes after organ transplantation, and acute rejection occurs within 2-60 days.

class I MHC gene product
See *major histocompatibility complex (MHC) class I molecule*.

class II MHC gene product
See *major histocompatibility complex (MHC) class II molecule*.

class switching
Process by which a *B cell* changes the class but not specificity of a given *antibody* it produces, e.g., switching from an *immunoglobulin M (IgM)* to an *immunoglobulin G (IgG)* antibody.
[3]

classical pathway (of complement activation)
Activation pathway involving *complement* components C1, C2 and C4 which, following fixation of C1q, e.g., by *antigen-antibody* complexes, produces the *classical pathway* C3 convertase C4b2a.
[3]
See also *alternative pathway (of complement activation)*.

clonal anergy
Form of *self-tolerance* developing as a consequence of negative selection during *thymic* selection processes. *Clone*s of *thymocyte*s whose antigen receptors [*T cell receptor*s *(TCR)*] bind with high *affinity* to *self-antigen*s in association with *major histocompatibility complex (MHC) molecule*s are inactivated.
[4]

clonal deletion
Process by which contact with *antigen* (e.g., self-antigen) at an early stage of *lymphocyte* differentiation leads to cell death by *apoptosis*.
[3]

clonal expansion
Proliferation of *B lymphocytes* and *T lymphocytes* activated by *clonal selection* in order to produce a *clone* of identical cells.

Note: Clonal expansion enables the body to have sufficient numbers of *antigen*-specific *lymphocyte*s to mount an effective *immune response*.

clonal indifference (ignorance)
Failure of *B* or *T cell*s expressing anti-self-*receptor*s to interact with *antigen* (e.g., by low

valency, low concentration, or sequestration of antigens; low receptor *avidity*; or lack of costimulatory molecules).

Note: This is the primary mechanism involved in the induction and maintenance of *self-tolerance*.

After [1]

clonal selection
Selection and *activation* by *antigen* of a *lymphocyte,* bearing a complementary *receptor*, which then proliferates to form an expanded *clone*.
[3]

clone
1. (n) Population of genetically identical cells or organisms having a common ancestor.
2. (vb) To produce such a population.
3. (n) Recombinant DNA molecules all carrying the same inserted sequence.
[5]

cluster determinant (CD)
Cluster of *antigen*s representating a cell surface marker with which *antibodies* react. Not to be confused with *cluster of differentiation (CD) antigen*.

cluster of differentiation (CD) **antigen**
Any of a family of molecular markers on cell surfaces that may be used operationally to define phenotype, origin, and *activation* state of the cell.

Note: The CD antigens expressed by a *T cell* vary with its stage of development and thus with its role in the *immune response*.

After [1]

coagulation system
Proteolytic cascade of *plasma* enzymes that triggers blood clotting when blood vessels are damaged.
After [2]

cognate T cell
*Helper T lymphocyte (Th) prime*d by the same *antigen* as the *B cell* to which it gives help.
After [2]

cold autoantibody type
Autoantibody that reacts optimally at low temperatures (0–5°C) with surface *antigen*s of *erythrocyte*s.

Note: It mediates *autoimmune hemolytic anemia* by either *cold agglutinin*s (cold hemagglutinin disease) or cold hemolysins (paroxysmal cold hemoglobinuria).

After [1]

collagen arthritis
Autoimmune model of *rheumatoid arthritis (RA)*, arising from combined *cellular immunity* and *humoral immunity* against collagen type II, and characterized by rapid and severe erosions of cartilage and bone.
After [12]

collectin
Any member of a structurally related family of calcium-dependent carbohydrate-binding proteins or *lectin*s containing collagen-like sequences, e.g., *mannose-binding lectin (MBL)*.
After [2]
See also *C-type lectin*.

colony stimulating factor (CSF)
Factor that permits the proliferation and differentiation of *hematopoietic* cells.
[3]

combinatorial diversity
Component of *antibody* and *T-cell receptor (TCR)* diversity that is generated by the recombination of *variable (V)*, *diversity (D*, for *immunoglobulin heavy chain*s, and for TCR β and δ chains), and *joining (J) gene* segments.
[3]
See also *V(D)J recombination*.

combinatorial joining
Merging of DNA segments generating new genetic information.

combined immunodeficiency
See *X-linked severe combined immune deficiency*.

common variable immunodeficiency
Relatively common deficiency in *antibody* production, of unknown pathogenesis but strongly associated with genes mapping within the *major histocompatibility complex (MHC)*.
Modified from [2]

Note 1: Characterized by reduced γ *globulin* levels, generally affecting all the *antibody* classes, but sometimes only *immunoglobulin G* (*IgG)*.

Note 2: Most patients have normal or near-normal numbers of *B-cell*s, which however do not differentiate into *plasma cell*s.

competitive inhibition assay
Method of measuring an *antigen* in a sample using a labeled species of the antigen as a competitive inhibitor of its binding in a specific *antigen-antibody reaction*.

complement
Group of approximately 20 *serum* proteinase precursors, some of which act in an

enzymatic cascade, producing effector molecules involved in *inflammation* (proteins C3a, C5a), *phagocytosis* (*opsonization*) (C3b), and cell lysis (C5b, C6–C9).
After [3]
See also *complement system*.

complementarity determining region (CDR)
Hypervariable amino acid sequence within *antibody* and *T-cell receptor (TCR) variable (V) region*s, which interacts with complementary amino acids on the antigen or *major histocompatibility complex (MHC)* – peptide complex.
After [3]

complement deficiency
Congenital deficiency in any of the various components of the *complement system*.

Note: Rheumatic disorders [mainly *systemic lupus erythematosus (SLE)*] are associated with deficiencies of the early components of the *classical pathway*. More than 30% of individuals with C2 deficiency and nearly 80% with either C3 or C4 deficiency have an *autoimmune* manifestation.

complement reaction
Physiological reaction to the presence of a foreign microorganism in which a cascade of enzymatic reactions, triggered by molecular features of the microorganism, result in lysis or *phagocytosis* of the foreign material.

complement receptor (CR)
Cell-surface protein that recognizes and binds *complement* proteins that have bound an *antigen*.

Note: Complement receptors on *phagocyte*s allow them to identify pathogens coated with complement proteins for uptake and destruction. Complement receptors include CR1, CR2, CR3, CR4, and the receptor for Clq.

After [2]

complement system
Group of *serum* proteins with the capacity to interact with each other when activated in a chain reaction which results in formation of a lytic complex and the release of several biologically active peptides of low relative molecular mass (*anaphylatoxin*s).

Note: The system can be activated by *antigen-antibody* complexes (*classical pathway*) and by other components, e.g., bacteria (*alternative pathway*). As an effector mechanism of the *humoral immune response*, the activated complement system facilitates *opsonization*, *phagocytosis* and lysis of cellular *antigen*s.

After [4]

concanavalin A (conA)
Hemagglutinin, isolated from jack bean (Canavalia ensiformis) meal, which reacts with polyglucosans in the blood of mammals, causing *agglutination*.

Note: Concanavalin A has been used to activate *T cell*s in vitro.

conformational epitope
Epitope on a protein *antigen* formed from several separate regions in the primary sequence of a protein brought together by protein folding.
[2]

congenic
Animals that only differ at a single genetic locus.
[3]

conjugate (in biochemistry)
1. Chemical species produced in living organisms by covalently linking two chemical moieties from different sources, for example, a conjugate of a *xenobiotic* with some group such as glutathione, sulfate, or glucuronic acid, to make it soluble in water or compartmentalized within the cell.
2. Material produced by attaching two or more substances together, for example, a conjugate of an *antibody* with a fluorochrome, or an enzyme.
[5]

conjunctivitis, allergic
Irritation of the ocular conjunctiva, resulting from the activation of conjunctival *mast cell*s by airborne *allergen*s such as pollens or house dust.

constant (C) domain
See *constant (C) region*.

constant (C) gene
Gene that encodes the *constant (C) region* of *immunoglobulin (Ig)* chains or *T-cell receptor (TCR)* chains.

constant (C) region
Part of an *immunoglobulin (Ig)* or *T-cell receptor (TCR)* that is relatively constant in amino acid sequence among different Ig or TCR molecules.
Note: In an *antibody* molecule the constant regions of each chain are composed of up to four C domains. The constant region of an antibody determines its general type of interaction.
After [2]
See also *variable (V) region*.

contact allergen
Substance that causes a skin *hypersensitivity* reaction by direct contact.

contact dermatitis
Skin *inflammation* that occurs when the skin's surface comes in contact with a substance originating outside the body.
Note: There are two kinds of contact dermatitis, irritant and *allergic*.

contact hypersensitivity
Immune response following skin contact with an *antigen*.

contact sensitivity
State of immunological *sensitization* in which an *eczema*tous epidermal reaction may occur when a *hapten* is applied to the skin of a sensitized individual.
[4]
See also *contact dermatitis*.

contact urticaria
Urticaria provoked by contact with inducing agents.
[4]

continuous epitope
See *linear epitope*.

conventional dendritic cell
Predominant type of *dendritic cell* active in *antigen* presentation to and *activation* of *naïve T cell*s.

convergent evolution
Independent evolution of similarity between molecules or between species.
[3]

convertase
Enzyme activity that converts *complement* protein into its reactive form by cleaving it.
Note: Generation of the *C3/C5 convertase* is the pivotal event in complement activation.
[7]

Coombs and Gell classification
See *Gell and Coombs classification.*

Coombs test
Diagnostic test using anti-*immunoglobulin (Ig)* to agglutinate *antibody*-coated *erythrocyte*s.
[3]
Note: The direct Coombs test, or direct antiglobulin test (DAT) refers to *agglutination* of a blood sample due to antibodies present on the erythrocyte surface. In the indirect Coombs test, or indirect antiglobulin test (IAT) antibodies free in the subject's *serum* are tested for their availability to agglutinate erythrocytes of known *antigenicity*.

coreceptor
Cell surface protein *receptor* that recognizes a substance bound to a primary receptor,

and binds to a signaling molecule that thereby enhances the activity of another receptor.

Note 1: Optimal *T cell activation* in an *immune response* depends on the involvement of relevant coreceptors occurring in a cluster with the *T-cell receptor*s *(TCR)*. The coreceptors are *CD4* or *CD8* proteins, which lie alongside the T-cell receptor in the plasma membrane. Only when both coreceptor and receptor bind the *major histocompatibility complex (MHC) molecule* – antigen complex simultaneously is the full set of intracellular effector molecules recruited and the signal pathway inside the cell maximally activated.

*Note 2: B-cell receptor*s *(BCR)* require the contributions of several coreceptors, notably CD19, CD21, and CD81 proteins, for full activation of intracellular signaling pathways.

corticosteroid

Any of the family of steroid molecules that are produced in the adrenal cortex, or their synthetic analogs.

Note: Corticosteroids can induce *apoptotic* cell death in *lymphocyte*s, especially developing *thymocyte*s. Therefore, they are useful anti-inflammatory, anti-*lymphoid* tumor, and *immunosuppressive* agents.

After [2]

costimulation

Delivery of a second signal, in addition to that of *antigen* binding or *antigen presentation*, that is required for *lymphocyte* proliferation.

Note 1: Co-stimulatory signals are delivered to *T cell*s by the co-stimulatory molecules, B7.1 and B7.2, related molecules (see *B7 molecule*) that are expressed on the surface of the *antigen-presenting cell (APC)*, and which bind the T cell surface molecule CD28.

*Note 2: B cell*s may receive co-stimulatory signals from common pathogen components such as *lipopolysaccharide (LPS),* from *complement* fragments, or from *CD40 ligand (CD40L)* expressed on the surface of an activated antigen-specific *helper T lymphocyte (Th)*.

counter-regulation hypothesis

Hypothesis that all types of infection early in childhood may protect against the development of *atopy* by driving the production of *cytokine*s such as *interleukin*-10 (IL-10) and *transforming growth factor-β (TGF-β)*, which downregulate both *Th1* and *Th2* responses.

[2]

Crohn disease

Chronic *inflammatory bowel disease (IBD)* thought to result from an abnormal overresponsiveness to commensal gut flora.

[2]

cross-matching

1. Test for determining the compatibility between the blood of a donor and that of a recipient before *transfusion*; the clumping of *erythrocyte*s indicates incompatibility.
2. Test for determining tissue compatibility between a transplant donor and the recipient before *transplantation*, in which the recipient's *serum* is tested for *antibodies* that may react with the *lymphocyte*s or other cells of the donor.
3. Process of performing one of these tests.

cross-presentation
cross-priming
Activation of *CD8+ lymphocyte*s by the presentation of exogenous *antigen*s in association with *major histocompatibility complex (MHC) class I* molecules.

Note 1: This is in contrast to normal activation of these lymphocytes (direct-*priming*) that results from presentation of endogenous antigens.

Note 2: The cells that cross-present antigens are the bone marrow-derived *antigen presenting cell*s *(APC)*. The form of antigen they monitor from tissues is predominantly cellular protein, acquired though *phagocytosis* and *macropinocytosis* and presented through two distinct pathways. In one pathway, antigen is transferred into the cytosol where it is degraded by *proteasome*s, and in the other, the antigen is hydrolyzed in the endocytic compartment

Note 3: Cross-presentation can lead to different outcomes, *tolerance* or *immunity*.
[13]

cross-priming
See *cross-presentation*.

cross‐reacting antibody
Any *antibody* that is able to react with an *antigen* that did not specifically stimulate its production.

Note: Cross‐reactions are usually weaker than the reaction of the antibody with the antigen that caused its production.

cross‐reacting antigen
1. Any *antigen* that is able to react with an *antibody* induced by a different antigen.

Note: The two antigens may share the same *antigenic determinant*s or carry determinants that are sufficiently alike stereochemically to enable the antibody to react with both.

2. Any antigen that has an identical structure in two strains of microorganism, so that antibody raised against one strain will react with the other strain.

cross-reactivity
1. Ability of an *antibody* or a *T cell*, specific for one *antigen*, to react with a second antigen.
2. Measure of relatedness between two *antigenic* substances, and (or) the polyspecificity of the antibody molecule (e.g., some *rheumatoid factor*s), or of the *T-cell receptor (TCR)*.

[4]

cross□sensitivity
State of immunological *hypersensitivity* to one substance that predisposes an individual to sensitivity to other substances that are related in chemical structure (*cross□reacting antigens*).

cross-tolerance (in immunology)
State of immunological *tolerance* to one substance produced by *priming* an animal with another substance that bears a *cross□reacting antigen*.

cryoglobulin
Immunoglobulin (Ig) that forms insoluble aggregates at temperatures below body temperature.

Note: Many cryoglobulins function as *autoantibodies* (e.g., *rheumatoid factor*). Cryoglobulins are found in lymphoproliferative (see *lymphoproliferation*) diseases, a number of *autoimmune diseases*, as well as chronic infections. They can cause vasculitic and secondary thrombotic manifestations (*cryoglobulinemic vasculitis*, *glomerulonephritis*).

After [1]

cryoglobulinemic vasculitis
Cutaneous or *systemic vasculitis* caused by cold-labile proteins (*cryoglobulins*, cryofibrinogen) that leads to increased viscosity, protein precipitation or gelatinification, *complement* activation, and endothelial cell damage, especially in the cold.

Note: Frequently associated with chronic hepatitis C or B infection, but can also be induced by other infections and malignancies.

After [1]

cryopyrin
See *NACHT domain-, leucine-rich repeat-, and PYD-containing protein 3*.

cryptic epitope
Any *epitope* that cannot be recognized by a *lymphocyte receptor* until the *antigen* has been broken down and processed or modified by *hapten* binding.
After [2]

cutaneous lymphocyte antigen (CLA)
Cell-surface molecule that is involved in *lymphocyte homing* to the skin in humans.
[2]

cutaneous T-cell lymphoma
mycosis fungoides
Malignant growth of *T cells* that home (see *homing*) to the skin.
[2]

cytokine
Any of a group of soluble small proteins released from a variety of cells, typically of the *immune system*, that affect cell behavior in an *autocrine* or *paracrine* fashion.

Note: Cytokines produced by *lymphocyte*s are known as *lymphokines*; those produced by *monocyte*s are called *monokines*. Other types of cytokine include *chemokines*, *growth factor*s, colony stimulating factors, *transforming growth factor*s, *interferon*s, *interleukin*s and *tumor necrosis factor*s.

cytokine capture assay
in vivo cytokine capture assay (IVCCA)
Method to detect *cytokine* release by injecting an animal with a neutralizing biotinylated *antibody* to the cytokine, which inhibits its utilization and allows its accumulation in the blood. Recovered cytokine-antibody complexes are then measured in an *enzyme-linked immonusorbent assay (ELISA)* with an antibody to a second epitope on the cytokine.

cytokine profile
Characteristic pattern of *cytokine* production associated with a defined immunological state.

cytokine release assay (CRA)
Method of quantifying *cytokine*s released by viable cells, using cytokine-specific *antibodies*.

cytolysis, immune
1. Cell lysis caused by a lesion produced by the action of *complement* proteins on the *antibody*-coated plasma membrane of a cell.
2. Cell lysis following plasma membrane reaction with *perforin*s released by *natural killer (NK) cell*s.

cytolytic T cell
See *cytotoxic T lymphocyte* (CTL, Tc).

cytomegalovirus (CMV)
visceral disease virus
Any of a group of highly *host*-specific slow growing herpes viruses that infect humans, monkeys, pigs or rodents, with the production of unique enlarged epithelial cells with intranuclear inclusions and often with a special affinity for the salivary glands.

Note 1: The virus specific for humans causes cytomegalic inclusion disease, and it has been associated with a syndrome resembling infectious mononucleosis.

Note 2: CMV is of most risk to unborn children of women who get CMV for the first time during pregnancy.

cytopenia
Decrease in the number of one or more types of blood cells.
See also *pancytopenia*.

cytotoxic
Causing damage to cell structure or function.
[5]

cytotoxic T cell
See *cytotoxic T lymphocyte* (CTL, Tc).

cytotoxic T lymphocyte (CTL, Tc)
CD8+ T cell
cytolytic T cell
cytotoxic T cell
killer T cell
Any of a subset of *T lymphocyte*s bearing the *CD8* surface marker and able to kill *target cell*s [infected somatic or tumor cells, recognized by the *antigen receptor* complex (*TCR/CD3*)] after induction of a specific *immune response* to the *antigen*s bound to *major histocompatibility complex (MHC) class I molecule*s.
Note: CD4+ T cells may also become cytotoxic.

cytotoxic T lymphocyte antigen 4 (CTLA-4)
CD152
High *affinity* receptor for *B7 molecule*s expressed on *T cell*s, binding of which inhibits T cell *activation*.
[7]
Note: Mutations in the gene encoding CTLA-4 have been associated with various *autoimmune disease*s.

cytotoxic T lymphocyte (CTL) **assay**
Assay based on quantitation of cell death caused by sensitized (see *sensitization*) *lymphocyte*s or splenocytes cultured with a fixed number of tumor or other *target cell*s that have been prelabeled with ^{51}Cr. The ^{51}Cr is taken up and reversibly binds to cytosolic proteins. When these target cells are incubated with sensitized lymphocytes, the target cells are killed and the ^{51}Cr is released.

cytotoxin
Substance with a specific toxic effect on certain cells.
Note: Major cytotoxins made by *cytotoxic T lymphocyte*s *(CTL, Tc)* and *natural killer (NK) cell*s that participate in the destruction of *target cell*s include *perforin*s, *granzyme*s, and granulolysins.

D gene
See *diversity (D) gene*.

DEC-205
CD205
Surface *antigen* characteristic of *dendritic cell*s.

DNA vaccination
DNA immunization
Injection of DNA into muscle, followed by its transcription and translation into a protein or proteins that elicit *antibody* and *T cell* responses.
See also *immunization*, *vaccination*.

DP, DQ, and DR molecules
*Major histocompatibility complex (MHC) class II molecule*s occurring on human *B lymphocyte*s and *antigen-presenting cell*s *(APC)*.

danger hypothesis
Hypothesis that suggests it is not foreignness of a molecule per se but rather its ability to cause cell damage or stress that induces an *immune response*. Often implicated in causation of *idiosyncratic drug reaction*s.

death receptor
death ligand receptor
Cell-surface *receptor* whose binding to extracellular *ligand*s stimulates *apoptosis* in the receptor-bearing cell through the *extrinsic pathway*.
See also *tumor necrosis factor (TNF)*.

death domain
Protein-interaction domain originally discovered in proteins involved in programmed cell death or *apoptosis*.

decay-accelerating factor (DAF)
CD55
Cell-surface molecule that protects cells from lysis by *complement*.

Note: The decay-accelerating factor binds to C3 *convertase*s of both the *alternative pathway* and *classical pathway of complement activation* and, by displacing Bb and C2b respectively, prevents their action. Its absence causes the disease paroxysmal nocturnal hemoglobinuria.

[2]

defensin
Any member of a family of oligopeptides made within the body, notably by *neutrophil*s and *macrophage*s, and having potent antimicrobial properties.

Note 1: Defensins play important roles against invading microbes. They act against bacteria, fungi, and viruses by binding to their membranes and increasing membrane permeability.

Note 2: Human defensins are classified into the α-defensins and β-defensins on the basis of their sequence homology and their cysteine residues.

After [1]

degranulation

Cell reaction that releases antimicrobial *cytotoxic* molecules and other substances (e.g., *histamine*) from secretory vesicles called granules found inside some cells.

Note: Degranulation occurs in several different cells involved in the immune system, including *granulocytes* (*neutrophils*, *basophils* and *eosinophils*), *mast cells*, and certain *lymphocytes* such as *natural killer (NK) cells* and *cytotoxic T cells*.

delayed-type hypersensitivity (DTH)
Gell and Coombs Type IV reaction
Form of *T cell*-mediated *immunity* in which the ultimate effector cell is the activated mononuclear *phagocyte* (*macrophage*); the response of DTH appears fully over 24 to 48 h. Previous exposure is required.

Note: Examples include response to Mycobacterium tuberculosis (*tuberculin test*) and *contact dermatitis*.

[4]

delayed-type hypersensitivity (DTH) **assay**
In vivo assay of *cell-mediated immune response,* elicited by *antigen* in the skin and mediated by *CD4+ Th1 cells*.

Note: DTH reactions are often divided into two phases which should be assessed in the assay: the *sensitization* phase, referring to the initial *immunization* with specific antigen, and the efferent or *challenge* phase of the DTH response, which usually follows 6 to 14 days after sensitization.

dendritic cell
interdigitating dendritic cell
interdigitating reticular cell
Ameboid cell that is *major histocompatibility complex (MHC) class II*-positive, *Fc receptor*-negative, and presents processed *antigens* to *T cells* in the T-cell areas of *secondary lymphoid* tissues.

Note 1: Dendritic cells are potent stimulators of T-cell responses. Nonlymphoid tissues also contain dendritic cells, but these are not able to stimulate T-cell responses until they are activated.

Note 2: There are three major sublasses of dendritic cells, *conventional dendritic cells*, *Langerhans cells*, and *plasmacytoid dendritic cells*.

Note 3: This is a different cell type from the *follicular dendritic cell*, which is *Fc receptor*-positive.

Note 4: Some authors also distinguish myeloid and lymphoid dendritic cells based on lineage.

[14]

Note 5: Some confusion in the classification of dendritic cells may arise from systems based on function, morphology, or lineage, and possibly species differences.

After [2, 3]

deposition, immune complex

Precipitation of *immune complex* in organs and tissues, often causing local *inflammation*.

Note: Immune complex deposition is a prominent feature of *systemic lupus erythematosus (SLE)*, *cryoglobulin*emia, *rheumatoid arthritis (RA)*, *scleroderma*, and *Sjögren syndrome*.

dermatitis
Inflammation of the skin showing redness, swelling, infiltration, scaling, and sometimes vesicles and blisters: *contact dermatitis* is due to local exposure and may be caused by irritation, *allergy*, or *photocontact dermatitis*.
Modified from [4]

dermatomyositis
Disease characterized by the presence of *inflammation* of the skin and muscles.

Note: Its cause is unknown, but it may be associated with a viral infection or some *autoimmune reaction* and may present also as paraneoplastic phenomena (see *paraneoplastic autoimmune syndrome*).

desensitization
Generally transient state of specific non-reactivity in a previously sensitized individual, resulting from repeated *antigen* exposures.
[4]
See also *sensitization*.

determinant
See *antigenic determinant*.

diabetes mellitus, insulin-dependent
See *diabetes mellitus type 1*.

diabetes mellitus type 1
Disease in which the β cells of the pancreatic islets of Langerhans are destroyed with the result that no insulin is produced.

Note: The disease is believed to result from an *autoimmune* attack on the β cells. It is also known as insulin-dependent diabetes mellitus (IDDM), as the symptoms can be ameliorated by injections of insulin.

[2]

diapedesis
Movement of blood cells, particularly *leukocyte*s, from the blood across blood vessel walls into tissues.
[2]

differential (in hematology)
Reported blood count that distinguishes the percentages of the different blood cells present.

differential splicing
Utilization and splicing of different exons from a primary RNA transcript in order to generate different mRNA sequences.
[3]

differentiation antigen
Cell surface molecule expressed at a particular stage of development or on cells of a given lineage.
[3]

DiGeorge syndrome
Immunodeficiency caused by a congenital failure in *thymic* development resulting in a lack of mature functional *T cell*s.
[3]

direct antiglobulin test (DAT)
See *Coombs test*.

direct Coombs test
See *Coombs test*.

discontinuous epitope
See *conformational epitope*.

disintegrin and metalloproteinase domain-containing protein 33 (ADAM33)
Member of the ADAM (A Disintegrin And Metalloproteinase domain) family of transmembrane proteins, possibly related to *asthma* susceptibility.

diversity (D) gene
Small segment of *immunoglobulin (Ig) heavy-chain* or *T-cell receptor* DNA between the *variable (V) gene* and *joining (J) gene* segments, coding for the third hypervariable region of the receptors.
See also *V(D)J recombination*.

domain (in molecular biology)
Structural element of a polypeptide.
[3]

dot plot
Two-dimensional graphical representation of individual data points.
Note: Often used to visualize the fluorescence and light scattering intensities acquired during *flow cytometry*.

double diffusion
See *Ouchterlony technique*.

double-negative cell
Immature T cell in the *thymus* that lacks expression of the two *coreceptors*, *CD4* and *CD8*.
Note: In a normal *thymus*, double-negative cells represent about 5% of *thymocyte*s.
[2]

double-positive cell
Immature T cell in the *thymus* that is characterized by expression of both *CD4* and *CD8 coreceptor* proteins.
Note: In a normal *thymus*, double-positive cells represent the majority (80%) of *thymocyte*s.
[2]
See also *pre-T cell*.

draining lymph node
Any *lymph node* that is downstream of a site of infection and thus receives *antigen*s and microbes from the site via the *lymphatic* system.
Note: Draining lymph nodes often enlarge enormously during an *immune response* and can be palpated; they were originally called swollen glands.
[2]

Draize test
1. ocular
Test for potential to cause irritation to the eye in which the test substance is applied directly to the eye of restrained rabbits.
Note: Widely criticized as unethical. Now often replaced with an acute eye irritation test using cadaveric chicken eyes.
2. skin
Test for the potential of a material to cause irritation or corrosion following local dermal application. Generally performed with rabbits.
[5]

drug-induced autoimmunity
Immune-mediated *idiosyncratic drug reaction* against *self-antigen*s.

drug-induced lupus
Idiosyncratic drug reaction similar in character to *systemic lupus erythematosus (SLE)* and having *anti-nuclear antibodies (ANA)*, but generally milder in nature and resolving when drug exposure is discontinued.

dyscrasia
See *blood dyscrasia*.

eczema

Acute or chronic skin *inflammation* with erythema, papules, vesicles, pustules, scales, crusts, or scabs, alone or in combination, of varied etiology.
[5]

edema
Presence of abnormally large amounts of fluid in intercellular spaces of body tissues.
[5]

effector cell
Cell that carries out an immune function, e.g., *cytokine* release, *cytotoxic*ity.
[3]

elicitation
Production of a cell-mediated or *antibody*-mediated *allergic* response by exposure of a sensitized individual to an *allergen*.
[4]
See also *cell-mediated immune response*.

embryonic stem (ES) **cell**
Embryonic cell that will grow continuously in culture and that retains the ability to contribute to all cell lineages.

Note 1: ES cells can be genetically manipulated in tissue culture and then inserted into mouse blastocysts to generate mutant lines of mice; often genes are deleted in ES cells by homologous recombination and the mutant ES cells are then used to generate gene *knockout mice*.

Note 2: ES cells may also be used to *clone* organisms.

endocytosis
Cellular ingestion of macromolecules by invagination of plasma membrane to produce an intracellular vesicle that encloses the ingested material.
[3]

endogenous
Antonym: exogenous
Produced within or caused by factors within an organism.
[5]

endosome
Intracellular smooth surfaced vesicle in which endocytosed (see *endocytosis*) material passes on its way to the *lysosome*s.
[3]

endotoxin
Pathogenic cell wall-associated lipopolysaccharides of Gram-negative bacteria.
[3]

enhancement (in immunology)
See *immune enhancement*.

enhancing antibody
Antibody that binds to an antibody-*antigen* complex or idiotypic-*anti-idiotypic antibody* complex and strengthens the interaction.

enterotoxin
Toxin affecting intestinal cells and thus causing food poisoning.

Note: Enterotoxins stimulate many types of *T cell*s by binding to *major histocompatibility complex (MHC) class II molecules* and the Vb domain [see *variable (V) domain*] of certain *T-cell receptor*s *(TCR)*. Enterotoxins have thus been referred to as *superantigen*s.

enzyme-linked immunosorbent assay (ELISA)
Procedure for detection or quantitation of an *antibody* or *antigen* using a *ligand* (e.g., an anti-*immunoglobulin*) conjugated to an enzyme that changes the color of a substrate.
[3]

Note 1: With a fixed amount of immobilized antigen, the amount of labeled antibody bound decreases as the concentration of unlabelled antigen is increased, allowing quantification of unlabelled antigen (competitive ELISA).

Note 2: With a fixed amount of one immobilized antibody, the binding of a second, labeled antibody increases as the concentration of antigen increases, allowing quantification of antigen (sandwich ELISA).

After [1]
See also *enzyme-linked immunospot (ELISPOT) assay*, *immunosorbent*.

enzyme-linked immunospot (ELISPOT) **assay**
Adaptation of *enzyme-linked immunosorbent assay (ELISA)* in which cells are placed over *antibodies* or *antigen*s attached to a plastic surface. The antigen or antibody traps the cells' secreted products, which can then be detected using an enzyme-coupled antibody that cleaves a colorless substrate to make a localized colored spot. This allows quantitation of the number of cells producing a given product such as a cytokine.

eosinophil
Circulating granular *leukocyte* (*granulocyte*) having prominent granules that stain specifically by eosin and containing numerous *lysosome*s.

Note 1: Eosinophils are important effector cells in immune reactions to *antigen*s that induce high levels of *immunoglobulin E (IgE) antibodies* (e.g., parasites).

Note 2: Eosinophils are also abundant at sites of *immediate-type hypersensitivity* reactions.

[4]

eosinophil chemotactic factor of anaphylaxis (ECF-A)

Cytokine that facilitates *anaphylaxis* and attracts *eosinophil*s during substrate release by *mast cell*s.

eotaxin
CCL11
CC chemokine that acts predominantly on *eosinophil*s.
[2]

epitope
Any part of a molecule recognized by *antigen receptor*s on *T*- or *B cell*s (T-cell epitopes or B-cell epitopes).
Note: A macromolecule can contain many different epitopes, each capable of stimulating production of a different specific *antibody*.
See also *antigenic determinant*.

epitope retrieval
antigen retrieval
Treatment of denatured *antigen* with heat or other agents in order to regenerate (unmask) lost *antibody*-binding capacity.

epitope spreading
Increase in the number of *epitope*s targeted by *autoantibodies* and (or) *T cell*s. The epitopes may be on the same *autoantigen* (intramolecular epitope spreading) and (or) on other autoantigens (intermolecular epitope spreading).
Note: This is a characteristic sign of progression of *autoimmune disease* from initial activation to a chronic state.
[1]

Epstein-Barr virus (EBV)
Virus responsible for infectious mononucleosis and Burkitt's lymphoma. This virus is used to immortalize human *B lymphocyte*s in vitro.
[3]

equivalence (in immunology)
Ratio of *antibody* to *antigen* at which *immunoprecipitation* of the reactants is virtually complete.
[3]

equivalence zone
Range of concentrations of *antigen* and *antibody* in which neither is in significant excess in a *precipitin* reaction.

erythema
Redness of the skin produced by congestion of the capillaries.
[5]

erythroblastosis fetalis
Two potentially disabling or fatal blood disorders in infants: *Rhesus (Rh) factor* incompatibility disease and *ABO blood group* incompatibility disease.

Note: The disorders are caused by incompatibility between a mother's blood and her unborn baby's blood, causing the mother's *immune system* to launch an *immune response* against the baby's *erythrocyte*s.

erythrocyte
Red blood cell.

erythropoiesis
Erythrocyte production.
[3]

erythropoietin
Glycoprotein hormone that stimulates the production of *erythrocyte*s by *stem cell*s in *bone marrow*.

Note: It is produced mainly by the kidneys and is released in response to decreased levels of oxygen in body tissue.

euglobulin
Member of a class of proteins insoluble in water but soluble in saline solutions.

exocytosis
Release of the content of an intracellular vesicle to the exterior of the cell.

Note: The vesicles make their way to the plasma membrane, with which they fuse to permit the contents to be released to the external environment.

[7]

exotoxin
Pathogenic protein secreted by bacteria.
[3]

experimental allergic encephalomyelitis (EAE)
See *encephalomyelitis, experimental allergic*.

extravasation
Movement of cells or fluid from within blood vessels to the surrounding tissues.
[2]

extrinsic allergic alveolitis
See *hypersensitivity pneumonitis (HPS)*.

extrinsic pathway (of apoptosis)
Apoptotic mechanism triggered by extracellular *ligand*s binding to specific cell-surface receptors (*death receptor*s), which then signal the cell to undergo programmed cell

death.
[2]
See also *intrinsic pathway (of apoptosis)*.

exudate
Extravascular fluid containing proteins and cellular debris that accumulates during *inflammation*.
[3]

Fab fragment
Monovalent *antigen*-binding ('ab') fragment obtained following papain digestion of *immunoglobulin (Ig)*. It consists of an intact *light chain* and the N- terminal VH and C H1 domains of the *heavy chain*.
[3]

F(ab')2 fragment
Bivalent *antigen*-binding fragment obtained following pepsin digestion of *immunoglobulin*. Consists of both *light chain*s and the N-terminal part of both *heavy chain*s linked by disulfide bonds.
[3]

Note: Because it lacks the *Fc fragment* it does not bind the *Fc-receptor*, e.g., in flow cytometry.

Fc fragment
Crystallizable, non-*antigen*-binding fragment of an *immunoglobulin (Ig)* molecule obtained following papain digestion. Consists of the C-terminal portion of both *heavy chain*s, responsible for binding to *Fc receptor*s and *complement* factor C1q.
[3]

Fc receptor
*Receptor*s expressed on a wide range of cells, interacting with the Fc portion (see *Fc fragment*) of *immunoglobulin*s *(Ig)* belonging to various *isotype*s.

Note: Membrane-bound Fc receptors mediate different effector functions (e.g., *endocytosis*, *antibody-dependent-cellular cytotoxicity (ADCC)*) and induce mediator release. Both the membrane-bound and soluble forms of Fc receptors regulate *antibody* production by *B lymphocyte*s.

After [4, 15]

Fc region
See *Fc fragment*.

Fd fragment
Heavy chain portion of an *immunoglobulin (Ig)* N-terminal to the papain hydrolysis site, after reduction and separation of the *light chain* portion.
See also *Fab fragment*.

fMLP peptide
Formyl-methionyl-leucyl-phenylalanine, a chemoattractant (see *chemotactic factor*, *chemotaxis*) derived from degradation of bacterial or mitochondrial proteins. It causes *neutrophil activation*.

Foxp3
Transcription repressor that is specifically expressed in *CD4+CD25+ T cell*s.
Note: Mutations in the FOXP3 gene may lead to an *autoimmune* syndrome called IPEX *(immunodysregulation–polyendocrinopathy–enteropathy, X-linked)*.
[1]

Fv fragment
Variable (V) region fragment of an *antibody heavy chain* or *light chain*.
[3]

familial cold autoinflammatory syndrome (FCAS)
Episodic *autoinflammatory disease*, induced by exposure to cold, and caused by mutations in the gene CSA1, encoding *cryopyrin*.
After [2]

familial hemophagocytic lymphohistiocytosis (FHL)
Progressive and potentially lethal inflammatory disease caused by an inherited deficiency of *perforin*.
Note: Large numbers of *polyclonal CD8+ T cell*s accumulate in *lymphoid tissue* and other organs, and this is associated with activated *macrophage*s that phagocytose (see *phagocytosis*) blood cells, including *erythrocyte*s and *leukocyte*s.
After [2]

farmer's lung
Hypersensitivity disease caused by the interaction of *immunoglobulin G (IgG) antibodies* with large amounts of an inhaled *allergen* in the alveolar wall of the lung, causing alveolar wall *inflammation* and compromising gas exchange.
After [2]

Fas
Cd95
Member of the *tumor necrosis factor (TNF) receptor* gene family. Engagement of Fas on the surface of the cell by the Fas *ligand* (CD178) present on *cytotoxic* cells, can trigger *apoptosis* in the Fas-bearing *target cell*.
[3]

fetal antigens
Human cancer cell *antigen*s, which *cross-react* serologically (see *serology*) with antigens normally expressed by embryonic tissue, e.g., *carcinoembryonic antigen (CEA)*, or α*-fetoprotein (AFP)*.

After [16]

fetal tolerance
Lack of *rejection* of a fetal *allograft* carrying paternal *major histocompatibility complex (MHC)* and *minor histocompatibility antigen*s that differ from those of the mother.

fibrinolysis
Enzymatic lysis of a fibrin clot.

fibrinolytic
Pertaining to, characterized by, or causing the breakdown of fibrin (*fibrinolysis*), usually by the action of plasmin.

fibroblast
Connective tissue cell that produces collagen and plays an important part in wound healing.
[3]

first line of defence
Surface tissues, notably the skin, respiratory tract and gastrointestinal tract.

Note1: These tissues are rich in *immunocompetent* cells that form a first line of defence by recognizing pathogens, destroying them with secretory *antibodies*, or preventing their intrusion into the organism.

Note 2: Internal organs may also have a first line of defence, e.g., the microglia have been considered as a first line of defence against brain infections.

flow cytometry
Method of sorting and measuring types of cells by fluorescent labeling of markers on the surface of the cells. It is sometimes referred to as Fluorescence-Assisted (or Activated) Cell Sorting (FACS) analysis.

fluorescein isothiocyanate (FITC)
Green fluorescent dye used to 'tag' *antibodies* for use in *immunofluorescence*.
[3]

fluorescence-activated cell sorting (FACS)
Fluorescence-assisted cell sorting
See *flow cytometry*.

fluorescent antibody
*Antibody conjugate*d to a fluorescent dye such as *fluorescein isothiocyanate (FITC)*.
[3]

follicular dendritic cell
Major histocompatibility complex (MHC) class II-negative *Fc receptor*-positive *dendritic cell* which bears *immune complex*es on its surface and is probably involved in the

generation of *antibody*-secreting cells and maintenance of *B-cell* memory (see *memory cell*) in *germinal center*s.

Note: This is a different cell type from the *dendritic cell*.

[3]

footpad test

Test for *allergic contact dermatitis* in which the test substance is injected into the front footpad of a Guinea pig and *challenge* is performed 7 days later.

Forssman antigen

Glycolipid *heterophile antigen* (globopentosylceramide) expressed on cell surfaces during embryonic and adult life in rodents and other mammals, and found in many pathogens, but probably not in humans.

Note 1: Anti-Forssman *antibodies* directed against the terminal sugar moiety are commonly found in plasma and may be involved in *Guillain–Barré syndrome (GB).*

Note 2: Anti-Forssman antibodies reportedly disrupt tight junction formation, apical-basal polarization, and cell adhesion.

After [17]

framework region

One of several relatively conserved amino acid sequences that flank the *hypervariable region*s in *immunoglobulin (Ig)* and *T-cell receptor (TCR) variable (V) region*s and maintain a common overall structure for all V region domains.

[3]

Freund's adjuvant

Complete Freund's *adjuvant* is an emulsion of aqueous *antigen* in mineral oil that contains heat-killed Mycobacteria.

Note 1: Incomplete Freund's adjuvant lacks the Mycobacteria.

Note 2: It can cause painful local *inflammation* and should be used with care.

After [3]

γ:δ T cell

Lymphocyte whose *T-cell receptor (TCR)* is a heterodimer of a γ chain and a δ chain.

See *γ:δ T-cell receptor*.

γ:δ T-cell receptor

T-cell receptor (TCR) composed of two different glycoprotein chains, designated γ and δ, assembled in a γ:δ heterodimer.

Note: Cells bearing these *receptor*s are called *γ:δ T cell*s. The group of γ: δ T cells is much less common than *α:β T cell*s, and usually found in the gut *mucosa*, in a population of *lymphocytes* known as *intra-epithelial lymphocyte*s (*IEL*s).

γ-interferon (IFN-γ)

Member of a group of *cytokine*s, the *interferon*s, which has as its primary action the

activation of *macrophage*s and can induce cells to resist viral replication.

Note: γ-interferon is a product of *CD4+ Th1* cells, *CD8+ T cell*s, and *natural killer (NK) cell*s.

G protein

Any member of a family of guanine nucleotide-biding proteins that binds GTP, converts it to GDP, and interacts with so-called G protein-coupled *receptor*s in the process of cell *signal transduction*.

Note: There are two kinds of G protein, the heterotrimeric (α, β, γ) receptor-associated G proteins, and the small G proteins, such as Ras and Raf, that act downstream of many transmembrane signaling events.

gp120

Viral glycoprotein, non-covalently associated with gp41 in the viral envelope of *human immunodeficiency virus (HIV)*.

Note: The gp120 portion of the glycoprotein complex binds with high *affinity* to the cell-surface molecule *CD4*. Before fusion and entry of the virus, gp120 must bind to a *coreceptor* in the membrane of the host-cell, for instance *chemokine receptor*s (mainly CCR5).

gammaglobulin

One of a group of *serum* proteins, mostly *immunoglobulin*s *(Ig)*, which have the greatest mobility towards the cathode during electrophoresis.

After [3]

gamma-interferon

See *γ-interferon (IFN-γ)*.

ganglioside

Member of a group of glycolipid components of all vertebrate cell membranes that are expressed at high densities in peripheral nervous tissues.

Note: Gangliosides are targets of *autoantibodies* in *autoimmune* peripheral neuropathies (e.g. anti-GM1, -GQ1b, -GD1b). Induced by infection, *natural autoantibodies* cross-reacting with gangliosides may become pathogenic after *affinity maturation* and *class switching*.

[1]

gastritis, autoimmune

Autoimmune-mediated destruction of the gastric *mucosa* that may result in the development of *pernicious anemia*.

Note: Autoimmune gastritis is associated with *autoantibodies* to H^+/K^+-ATPase of gastric parietal cells as well as *autoantibodies* to the intrinsic factor produced by these cells.

[1]

Gell and Coombs classification

Classification of immune mechanisms of tissue injury into four types: type I, *immediate-type hypersensitivity* reactions, mediated by interaction of *immunoglobulin E (IgE) antibody* and *antigen* causing the release of *histamine* and other mediators; type II, antibody-mediated *hypersensitivity* reactions, due to antibody-antigen interactions on cell surfaces; type III, *immune complex*, local or general inflammatory responses due to formation of circulating immune complexes and their deposition in tissues; and type IV cell-mediated hypersensitivity reactions, initiated by sensitized *T lymphocyte*s either by release of *lymphokine*s or by T-cell-mediated cytotoxicity [see *cytotoxic T lymphocyte (CTL)*].

gene knockout
gene targeting
Method of disabling a specific gene by homologous recombination with an introduced DNA construct designed for that purpose.
See also *knockout*, *knockout mouse*.

gene rearrangement
Structural alteration in a chromosome that changes the order of its genetic loci, occurring by DNA recombination, e.g., during development or in some cancers.

Note: In *immunology*, it refers to recombination of gene segments in *immunoglobulin (Ig)* and *T-cell receptor (TCR)* loci to produce a functional *variable (V) region* sequence.

gene targeting
See *gene knockout*.

germ-free
gnotobiotic
Descriptor applied to animals (usually mice) raised in the complete absence of intestinal and other microorganisms.

Note: Such mice have very depleted *immune system*s, but they can respond normally to any specific *antigen*, provided it is mixed with a strong *adjuvant.*

germ line (in immunology)
Refering to genes in their unrearranged state rather than those rearranged for production of *immunoglobulin (Ig)* or *T-cell receptor (TCR)* molecules.
After [7]

germinal center
Discrete area within *lymph node*s and *spleen* where *B-cell maturation* and *memory* development occur.
[3]

giant cell
Large multinucleate cell derived from fused *macrophage*s and often present in *granuloma*s.

[3]

glomerulonephritis
Any of a group of kidney diseases involving *inflammation* of the renal glomeruli (see *glomerulus*), often as a result of *antibody-antigen* complexes that localize in the kidney.
Note: Acute *nephritis* is marked by blood in the urine.

glomerulonephropathy
glomerulopathy
Disease of the renal *glomeruli*, which may show either thickening of the glomerular basement membrane due to the accretion of proteins or a minimal change disease, in which there is functional damage but little structural change by light microscopy.
[1]

glomerulus
Tuft or a cluster, as of a plexus of capillary blood vessels or nerve fibers (e.g., capillaries of the filtration apparatus of the kidney).
[5]

glucocorticoid
Any member of the group of endogenous hormones that play an important role in the normal regulation of the *immune system* and act as physiological *immunosuppressant*s involved in the control of immune and inflammatory hyperactivity during a stress response.

glutamic acid decarboxylase (GAD)
Main *autoantigen* in *diabetes mellitus type 1* and stiff-person syndrome (a neurological *autoimmune disease*).
Note: GAD is localized in pancreatic β cells and γ-aminobutyric acid-responsive (GABAergic) neurons.
[1]

gluten
1. Any of the prolamins found in cereal grains, especially the prolamins in wheat, rye, barley, and possibly oats, which cause digestive disorders, notably *celiac disease*.
2. In wheat, mixture of water-insoluble proteins, including gliadins, that give wheat dough its elastic texture.

gluten enteropathy
See *celiac disease*.

gluten intolerance
See *celiac disease*.

gnotobiotic
See *germ-free*.

Goodpasture syndrome
Goodpasture disease
Autoimmune disease of humans in which *glomerulonephritis* and pulmonary hemorrhage are produced by *complement*-mediated tissue damage caused by *antibodies* directed against the renal glomerular and alveolar basement membranes.

graft
Tissue *transplant*ed into a *host* or surgically moved from one site to another within an individual.
See also *allograft*, *autograft, isograft*, *xenograft*.

graft rejection
Destruction of *graft*ed tissue by *host lymphocyte*s following an *adaptive immune response*.
See also *rejection*.

graft-versus-host disease (GVHD)
Disease that occurs following *bone marrow transplantation* between genetically non-identical people and in which mature *T cell*s in the transplanted bone marrow attack and destroy the recipients's tissues.
See also *graft-versus-host (GVH) reaction*.

graft-versus-host (GVH) **reaction**
Reaction occurring when *T lymphocyte*s present in a *graft* recognize and attack *host* cells.
[3]

granulocyte
Myeloid cell containing cytoplasmic granules (i.e., *neutrophil*s, *eosinophil*s and *basophil*s).
[3]

granulocyte colony-stimulating factor (G-CSF)
Hematopoietic (see *hematopoiesis*) factor augmenting the production of *neutrophil*s in the *bone marrow*.

granulocyte–macrophage colony-stimulating factor (GM-CSF)
Cytokine that stimulates production of *granulocyte*s and *monocyte*s from *stem cell*s.

granulocytopenia
Decreased circulating *granulocyte*s.
See also *agranulocytosis.*

granuloma

Mass or nodule of granulation tissue, with actively growing *fibroblast*s and capillary buds, characterised by the presence of aggregates of modified *macrophage*s resembling epithelial cells (epithelioid histiocytes), and *lymphocytes,* surrounded by a rim of giant multinucleate cells, either of the *Langerhans* or foreign body type.

Note: Granuloma is due to a chronic inflammatory process associated with infectious disease, such as tuberculosis, syphilis, *sarcoidosis*, leprosy, lymphogranuloma, etc., or with invasion by a foreign body.

After [18]

granzyme
Member of a family of serine esterases present in the granules of *cytotoxic T lymphocyte*s and *natural killer (NK) cell*s. They induce *apoptosis* in the *target cell* that they enter through *perforin* channels inserted into the target cell membrane by the cytotoxic lymphocyte.
[3]

Graves disease
Hyperthyroidism associated with diffuse hyperplastic goitre resulting from production of a *thyroid-stimulating hormone receptor (TSHR)*-binding *autoantibody*.

growth factor
Any of a group of biologically active poly-peptides that function as hormone-like regulatory signals, controlling the growth and differentiation of responsive cells.

Guillain-Barré syndrome (GBS)
Type of *idiopathic* polyneuritis in which *autoimmunity* to peripheral nerve myelin leads to a condition characterized by chronic demyelination of the spinal cord and peripheral nerves.
[7]

guinea pig maximization test (GPMT)
Skin sensitization test for *allergic contact dermatitis* in which shaved guinea pig skin is exposed to intradermal injections of a test agent together with complete *Freund's adjuvant*, followed by an occlusive patch for boosting (see *booster*) for 48 h beginning on day 7, and *challenge*d on day 21.

gut-associated lymphoid tissue (GALT)
Lymphoid cells and tissues lining the *mucosa* that seem to serve as the first point of *antigen* contact via this route, including *Peyer's patch*es, the *appendix*, *tonsil*s, adenoids and mesenteric *lymph node*s.

Note: Large aggregates of GALT have distinct B cell follicles and T cell areas. Antigen-presenting accessory cells are also present.

H-chain
See *heavy chain*.

H-2
Region of mouse chromosome 17 coding the *major histocompability complex (MHC)*.

H-2 complex
Mouse *major histocompatibility complex (MHC)* coded by *H-2*.

hairy cell leukemia
B cell neoplasm, usually occurring during middle age, constituting about 2% of all *leukemia*s and responding well to chemotherapy. The neoplastic cells have fine, hairlike surfaces.
After [19]

haplotype
Set of allelic (see *allele*) variants present at a given genetic region.
[3]

hapten
Low-molecular-mass molecule that is not itself *immunogen*ic unless complexed with a carrier, such as a protein. Once bound, it presents an *epitope* that can cause the *sensitization* of *lymphocyte*s.
[5]

haptenic
Able to act as a *hapten*.

Hashimoto thyroiditis
chronic lymphocytic thyroiditis
Autoimmune disease where the body's own *antibodies* attack the cells of the thyroid.

hay fever
pollenosis
Allergic condition affecting the mucous membranes of the upper respiratory tract and the eyes, characterized by nasal discharge (see *rhinitis*), sneezing, and itchy, watery eyes; and usually caused by an abnormal sensitivity to airborne pollen.

heat-shock proteins
Evolutionarily conserved proteins, found in many organisms, that are induced upon exposure of cells to various types of stress, including heat, oxidative or hypoxic stress, and deprivation of nutrients or essential ions.

heavy chain
H-chain
Larger of the two types of polypeptide chain found in *immunoglobulin (Ig)* molecules.
Note: Each heavy chain is linked by disulfide bonds to a light chain and to another, identical heavy chain. Each heavy chain consists of an *Fc fragment* and an *Fd fragment*. Heavy chains carry the *antigenic determinant*s that

differentiate the various immunoglobulin classes.

helper cell
See *helper T lymphocyte (Th).*

helper T lymphocyte (Th)
helper cell
helper T cell
T helper cell
Member of a subclass of *T lymphocyte*s that provides help (in the form of *cytokine*s and/or cognate interactions) necessary for the expression of effector function by other cells in the *immune system*.

Note: Helper T-cells recognize *antigen* in association with *major histocompatibility complex (MHC) class II* gene products. Depending on their capacity to produce various cytokines, one can functionally differentiate *Th1* [*interleukin*-2- (IL-2-) and *IFN-γ*-producing] and *Th2* (interleukins IL-3-, IL-4- and IL-6-producing) cells.

Modified from [4]

hemagglutination
Agglutination of *erythrocyte*s.

hemagglutinin
Any molecule that agglutinates *erythrocyte*s.
See also *agglutination*.
[3]

hematopoiesis
Production of *erythrocyte*s, *leukocyte*s and *platelet*s.
[3]

hematopoietic stem cell
Self-renewing *stem cell* that is capable of giving rise to all of the formed elements of the blood (i.e., *leukocyte*s, *erythrocyte*s and *platelet*s).
[3]

hemolytic anemia
Anemia resulting from the lysis of *erythrocyte*s.

hemolytic plaque assay
See *antibody-forming cell (AFC) assay*.

heparin-induced thrombocytopenia (HIT)
Most frequent *antibody*-mediated drug-induced *thrombocytopenia*, which occurs in 1-2 % of patients treated with heparin intravenously for longer than four days.

Note: This disease is mediated by antibodies to complexes formed between

heparin and the endogenous *platelet* factor 4 (PF4).
[1]

hereditary angioneurotic edema
Clinical name for a genetic deficiency of the *C1 inhibitor* of the *complement system*.
Note: In the absence of C1 inhibitor, spontaneous activation of the complement system can cause diffuse fluid leakage from blood vessels, the most serious consequence of which is epiglottal swelling leading to suffocation.
[2]

heteroantigen
heterogenetic antigen
One of a set of identical or similar *cross-reacting antigen*s shared by several species (e.g., *Forssman antigen*). *Antibodies* produced against one of these antigens will also react with the other antigens of the set even though these are derived from a different species; such antibodies are also called *heterophile antibodies*.
After [20]

heterologous antibody
Antibody derived from another indivual of the same species or another species.
See also *autologous antibody*.
After [21]

heterologous antigen
Antigen that reacts with an *antibody* other than the one whose formation it induced.

heterophagy
Digestion of exogenous material taken up by a cell by *phagocytosi*s or *pinocytosi*s, following fusion of the phagocytic or pinocytic vacuole with a *lysosome*.

heterophile antibody
heterophilic antibody
Antibody raised against an *antigen* from one species, which also reacts against antigens from other species.
Note 1: Heterophile antibodies are usually of low affinity and are a common cause of problems with *immunoassay*s.
Note 2: The existence of such antibodies explains observations of the presence of antibody against antigens from a variety of species without *immunization*.
Note 3: Heterophile antibodies commonly arise from viral infection.
See also *Forssman antigen*.

heterophile antigen
heterophilic antigen
Antigen that stimulates production in a vertebrate of *antibodies* capable of reacting with tissue components having related antigens in a wide range of other species.
See also *Forssman antigen*.

heterozygous
Possessing different *allele*s at a given locus on the two homologous chromosomes.
[3]

high endothelial venule (HEV)
Specialized venule in *lymphoid tissue*s that has walls permeable to migrating *lymphocyte*s, allowing them to move from blood into the lymphoid tissues.

highly active antiretroviral therapy (HAART)
Approach to the treatment of *acquired immune deficiency syndrome (AIDS)* patients involving a combination of nucleoside analogs, which prevent reverse transcription, with drugs that inhibit responses to the virus.
After [2]

high-mobility group box (HMGB) **protein**
Any of a group of universal sensors of nucleic acids, required for the induction of transmembrane and cytoplasmic receptor-mediated *innate immune response*s.
After [22]

hinge region
Amino acids between the *Fab* and *Fc* regions of *immunoglobulin (Ig)* that permit flexibility of the molecule.
[3]

histamine
2-(1H-imidazol-4-yl)ethan-1-amine
Amine derived from histidine by decarboxylation and released from cells in the *immune system*, especially *mast cell*s, as part of an *allergic* reaction.
Note: It is a powerful stimulant of gastric secretion, constrictor of bronchial smooth muscle, and vasodilator.
[5]

histaminosis
Histamine intolerance, which may contribute to food intolerance as part of a *pseudoallergic reaction*.

histocompatibility
Relationship between a tissue or organ donor and a recipient who have sufficient similarity in *major histocompatibility complex (MHC) antigen*s to avoid *rejection* of a *graft*.

histoincompatibility
Relationship between a tissue or organ donor and a recipient who have sufficient differences in *major histocompatibility complex (MHC) antigen*s to cause *rejection* of a *graft*.

hives
nettle rash
urticaria
Vascular reaction pattern of the skin marked by the transient appearance of smooth, slightly elevated patches (*wheal*s) that are either more red or more pale than the surrounding skin and are accompanied by severe itching.
Note: They are usually, but not always, caused by an *allergic* reaction to food or to a drug, but can also be induced by physical stimuli such as cold or exercise.

Hodgkin disease
Hodgkin lymphoma
Immune system tumor characterized by large cells called *Reed-Sternberg cell*s that derive from mutated B-lineage cells.
Note: Hodgkin disease exists in at least two forms, Hodgkin lymphoma and nodular sclerosis.
[2]

homing
Movement of *leukocyte*s to specific locations in the body.

homing receptor
Cell surface molecule that directs *leukocyte*s to specific locations in the body.
[3]

homocytotropic antibody
Antibody that binds preferentially to cells from the same species rather than to cells from other species.
After [21]
See also *autologous antibody*, *heterologous antibody*, *heterophile antibody*.

homozygous
Possessing the same *allele* at a given locus on the two homologous chromosomes.
[3]

horror autotoxicus
Term (Latin: dread of self-poisoning) introduced by Paul Ehrlich (1902), to describe the body's innate aversion to immunological self-destruction.

host (in immunology)
Recipient of foreign cells or tissue, or of an infectious agent.

host defense
Ability of an individual to resist invasion by opportunistic agents and production of disease associated with exposure to microorganisms, foreign tissue, and particulates, as well as certain types of neoplasia. Host defense may be either nonspecific (*innate* or

natural immunity) or specific (*adaptive* or *acquired immunity*) in nature.

Note: Immunological defense may involve *chemotaxis*, *phagocytosis*, reaction with i*mmunoglobulin*s *(Ig)* and (or) with *complement*, and *T cell cytotoxicity*.

host-resistance assay
Evaluation of *host resistance* in rodents to in vivo *challenge* with an infectious organism under normal conditions and after pharmacological and nutritional alterations of the *immune system*.

human immunodeficiency virus (HIV)
Causative agent of *acquired immune deficiency syndrome (AIDS)*.

Note 1: HIV is a retrovirus of the lentivirus family that selectively infects *macrophage*s and *CD4+ T cells*, leading to their slow depletion, eventually resulting in *immunodeficiency*.

Note 2: There are two major strains of the virus, HIV-1 and HIV-2, of which HIV-1 causes most disease worldwide. HIV-2 is endemic to West Africa but is spreading.

[2]

humanized antibody
Genetically engineered *monoclonal antibody* of non-human origin in which all but the *antigen*-binding *complementarity determining region (CDR)* sequences have been replaced with sequences derived from human antibodies.

Note: This procedure is carried out to minimize the *immunogen*icity of *therapeutic, monoclonal antibodies*.

[3]

human leukocyte antigen (HLA)
Antigen coded by genes of the human *major histocompatibility complex (MHC)*.

Note 1: Human HLA-A, -B and -C (resembling mouse H-2K, D and L) are *MHC class I* molecules, whereas HLA-DP, -DQ and -DR (resembling mouse I-A and I-E) are *MHC class II* molecules.

Note 2: The genes for HLAs are situated on chromosome 6.

After [1]

human leukocyte antigen (HLA) **polymorphism**
Discontinuous genetic variation in the *major histocompatibility complex (MHC)* that results in the occurrence of several different forms of MHC molecules among people.

Note: Specific HLA polymorphisms are associated with a number of diseases, e.g., HLA-B27 is associated with ankylosing spondylitis, psoriatic arthritis, *rheumatoid arthritis (RA)*, etc., and some chemical sensitivities.

human leukocyte antigen (HLA) **type I**
Molecules that enable the body to recognize infected cells and tumor cells and destroy them with *cytotoxic T lymphocyte*s *(CTL)*.

Note: HLA type I molecules are made by all nucleated cells in the body, possess a

deep groove (see *peptide-binding groove*) that can bind peptide *epitope*s, typically 8-11 amino acids long, from endogenous *antigen*s; and present HLA type I/peptide complexes to *CD8+ lymphocyte*s that have a complementary shaped *T-cell receptor (TCR)*.

human leukocyte antigen (HLA) **type II**
Molecules that enable *CD4+ lymphocyte*s to recognize *epitope*s of exogenous a*ntigen*s and discriminate self from *non-self*.

Note: HLA type II molecules are made by *antigen-presenting cells (APC)*, such as *dendritic cell*s, *macrophage*s, and *B lymphocyte*s, possess a deep groove (see *peptide-binding groove*) that can bind peptide *epitope*s, typically 10-30 amino acids long but with an optimum length of 12-16 amino acids, from exogenous antigens; and present HLA type II/peptide complexes to CD4+ lymphocytes that have a complementary shaped *T-cell receptor (TCR)*.

humoral
Pertaining to extracellular fluid such as *plasma* and *lymph*.

Note: The term *humoral immunity* is used to denote *antibody*-mediated *immune response*s such as *phagocytosis* and activation of the *complement system*.

Modified from [3]

humoral immune response
Immune response in which specific *antibodies* induce the effector functions (such as *phagocytosis* and activation of the *complement system*).
[1]

humoral immunity
Specific *immune response* that is mediated primarily by humoral factors circulating in solution in the *blood plasma* and *lymph* (i.e., *antibodies* and *complement*).

Note: The induction of the *humoral immune response* generally requires the cooperation of cellular immune mechanisms.

humorally-mediated immunity (HMI)
See *humoral immunity*.

hybridoma
Hybrid cell line obtained by fusing a lymphoid tumor cell with a *lymphocyte*. The resultant cell line has both the immortality of the tumor cell and the effector function (e.g., *monoclonal antibody* secretion) of the lymphocyte.
[3]

hygiene hypothesis
See *counter-regulation hypothesis*.

hypergammaglobulinemia
Increase of *gammaglobulin*s in the blood by paraproteinemia or increased production of

immunoglobulins (Ig).
[1]

hyperimmunoglobulin E syndrome
Job syndrome
Rare *primary immunodeficiency* syndrome characterized by recurrent severe staphylococcal skin abscesses (hence Job syndrome), lung infections, and markedly elevated *serum immunoglobulin E (IgE)* levels.

hyperimmunoglobulin M syndrome (HIGM)
Primary *T cell* defect due to mutations in the *CD40 ligand (CD40L)*, characterized by recurrent (opportunistic) infections and very low levels of *immunoglobulin G (IgG)* and *immunoglobulin A (IgA)*.

Note: Autoimmune manifestations (e.g., *cytopenia*, *arthritis*, sclerosing cholangitis) are often seen.

After [1]

hyperreactivity
Abnormally increased response to a stimulus.
[4]

hypersensitivity
State in which an individual reacts with *allergic* effects following exposure to a certain substance (*allergen*) after having been exposed previously to the same substance. It is sometimes used loosely for any increased response.

Note: Four types of hypersensitivity are recognized. Most common chemically induced allergies are type I [*immunoglobulin E- (IgE-*) mediated] and type IV (cell-mediated) hypersensitivity.

See also *allergy*, *Gell and Coombs classification*.
After [5]

hypersensitivity pneumonitis (HPS)
extrinsic allergic alveolitis
Immune-mediated inflammatory disease of the lung parenchyma caused by exposure to an inhaled chemical *allergen* or organic dust.
[4]

hypersensitization
Development of excessive immune reactivity to an *antigen*.

hypersusceptibility
Adverse immunological effects in an individual occurring under conditions of exposure to an *allergen* that result in no effects in the great majority of the population, or an individual exhibiting exaggerated effects in comparison with the great majority of those showing some adverse effects.
After [4]

hypervariable region
Amino acid sequence within the *immunoglobulin (Ig)* and *T-cell receptor (TCR) variable (V) region*s that shows the greatest variability and contributes most to the *antigen* or peptide-*major histocompatibility complex (MHC) molecule* binding site.
[3]

hypogammaglobulinemia
Immunodeficiency state marked by abnormally low levels of all classes of *immunoglobulin*s *(Ig)*, associated with increased susceptibility to infectious diseases.
Note: It may be primary (inherited), or secondary (acquired), or it may occur physiologically in normal *neonate*s.

hyposensitization therapy
Dermal application of a selected *allergen* to an *allergic* person in stepwise increasing dosage, with the aim of reducing the *immune system*'s tendency for the corresponding *allergic reaction*.

Ia antigen
I region-associated antigen
immune response-associated antigen
Isooantigen encoded by the Ia region of the mouse *major histocompatibility complex (H-2 complex)*.
Note 1: Ia *antigen*s are defined by serological methods (see *serology*) and are found predominantly on *B lymphocyte*s and *macrophage*s.
Note 2: This term is also used as a generic term for any *major histocompatibility complex (MHC) class II* antigen.
See also *immune response-associated (Ia) protein*.

idiopathic
Term that describes a "primary" symptom or disease in which no underlying cause or associated disorder can be found.
Note: In many cases, *autoimmune* processes are involved in the pathogenesis [e.g., idiopathic *Addison disease,* idiopathic *thrombocytopenic purpura* (ITP)].

idiopathic environmental intolerance
See *multiple chemical sensitivity*.

idiopathic thrombocytopenic purpura (ITP)
Thrombocytopenia of unknown cause, probably related to the production of anti-*platelet* antibodies, and leading to bruising (*purpura*).

idiosyncratic drug reaction (IDR)
Rare and unpredictable *adverse drug reaction* occurring only in susceptible individuals.
Note: A dose-reponse relationship may not be apparent within the dose range

used clinically.

idiotope
Epitope made up of amino acids within the *variable (V) region* of an *antibody* or *T-cell receptor (TCR)* that reacts with an anti-idiotope antibody.
After [3]

Note: The anti-idiotopic region of the anti-idiotope antibody may mimic the epitope-binding characteristics of the *antigen* without sharing any sequence homology.

See also *anti-idiotypic antibody*, *idiotype*.

idiotype
The combined *antigenic determinant*s (*idiotope*s) expressed in the *variable (V) region* of *immunoglobulin*s *(Ig)* of an individual that determine *antibody* specificity to a particular *antigen*.
See also *anti-idiotypic antibody*.
After [2, 102]

idiotype network
idiotypic network
Regulatory network based on interactions of *anti-idiotypic antibodies* and *idiotype*s present on *antibodies* and *T-cell receptor*s *(TCR)*, resulting in feedback inhibition of ongoing *B cell* or *T cell* responses.
After [1, 3]

immature (in immunology)
Describing cells that are not fully developed and unable to participate immediately in an *immune response*.

Note: Immature *B cell*s and *T cell*s migrate from their *primary lymphoid* sites (*bone marrow* and *thymus*) through the vascular and *lymphatic system*s to *secondary lymphoid* sites. These sites include the *spleen*, *lymph node*s, *tonsil*s, and *Peyer's patch*es in the intestine and *appendix*. The immature B cells and T cells mature only after they encounter an *antigen*.

immediate-type hypersensitivity
immediate-type allergy
type I hypersensitivity
Reaction provoked by re-exposure to an *antigen* (*allergen*) that causes *plasma cell*s to secrete *immunoglobulin E (IgE)* which binds to *Fc receptor*s on the surface of tissue *mast cell*s and blood *basophil*s, sensitizing them, so that later exposure to the same allergen cross-links the bound IgE, leading to *degranulation* and the secretion of pharmacologically active mediators such as *histamine*, *leukotriene*, and *prostaglandin* that act immediately on the surrounding tissues.

Note: The principal effects of these products are vasodilation and smooth-muscle contraction. The reaction may be either local or *systemic*. Symptoms vary from mild irritation to sudden death from *anaphylactic shock*.

immune adherence
Attachment of particulate *antigen* coated with C3b (see *complement*) to cells expressing C3b *receptor*s, which results in enhanced *phagocytosis* of bacteria by *macrophage*s.
After [7]

immune complex
Product of an *antigen–antibody* reaction, which may also contain components of the *complement system.*
[5]

immune complex disease
Illness resulting from deposition of *antigen-antibody* complexes in tissues.

immune deviation
Regulatory mechanism of the preferential activation of one aspect (cellular or humoral) of the *adaptive immune system* at the expense of the other.

Note: Although not a form of true *tolerance*, this regulatory mechanism may be involved in the induction and maintenance of *self-tolerance*.

After [1]

immune elimination
Removal of pathogens or tumor cells by the immune system; the first step of *immunoediting* of tumors.

immune enhancement
Therapeutic stimulation of the *immune response*, especially in tumor therapy.

immune equilibrium
State in carcinogenesis where there is an equilibrium between elimination of tumor cells by the *immune system* and growth of non-*immunogen*ic tumor cells; the second step in *immunoediting*.

immune escape
Biological feature of an infectious agent or of a tumor cell that prevents its elimination by the *immune system*. Such a feature can be acquired by a selection process. Immune escape is the third step in *immunoediting* of tumors.

immune evasion
Property of a pathogen that results in avoidance of attack by the *immune system*, e.g., because of reduced *phagocytosis*, lack of recognition by the *innate immune system*, or *suppression* of the *immune response*.

immune modulation
immunomodulation
Alteration of the *immune response* to alleviate harmful effects of the *immune system* or

to promote its activity by changes in regulatory factors; often part of deliberate therapeutic intervention.

immune regulation
immunoregulation
Capacity of the *immune system* to regulate itself so that an *immune response* does not become excessive and cause tissue damage, *autoimmune* reactions, or *allergic reaction*s.
[2]

immune reserve hypothesis
Hypothesis that the *immune response* involves multiple redundancies that are capable of compensating for acute reductions in certain immune functions.
Note: Such a reserve might prevent a serious reduction in *host resistance* after temporary *immunosuppression* of selected parameters [e.g., *natural killer (NK) cell* function].

immune response
Selective reaction of the body to substances that are foreign to it, or that the *immune system* identifies as foreign, shown by the production of *antibodies* and antibody-bearing cells or by a cell-mediated *hypersensitivity* reaction.
[5]
See also *cell-mediated immune response*.

immune response-associated (Ia) protein
Protein found in *antigen-presenting cell*s *(APC)* and *B lymphocyte*s in mice.
Compare *Ia antigen*.

immune response genes
Genes, including those within the *major histocompatibility complex (MHC)*, that together determine the overall level of *immune response* to a given *antigen*.
[3]

immune surveillance
immunosurveillance
Recognition, and in some cases elimination, of tumor cells by the *immune system* before they become clinically detectable.
[2]

immune system
Integrated network of organs, glands, and tissues that has evolved to protect the body from foreign substances, including bacteria, viruses, and other infection-causing parasites and pathogens.
Note: The immune system may produce *hypersensitivity* reactions that, in the extreme, can be fatal. If the immune system misidentifies normal body components as foreign, this leads to *autoimmune* disorders, such as

systemic lupus erythematosus (SLE), in which the body destroys its own constituents.
[5]

immune thrombocytopenic purpura
See *thrombocytopenic purpura, idiopathic (ITP)*.

immunity
Inherited, acquired, or induced *resistance* to infection by a specific pathogen.

immunization
Making an organism immune to a specific agent, such as an *allergen*, pathogen, or cancer cell.
See also *active immunization*, *passive immunization*.

immunoactivation
Activation of the *immune system* as a whole to react more rapidly to *antigen*s.

immunoactivator
Substance that activates the *immune system* as a whole to react more rapidly to *antigen*s.

immunoadsorption
Method for removal of *antibody* or *antigen* by allowing it to bind to a corresponding antigen or antibody immobilized in the solid phase.
After [3]

immunoassay
Ligand-binding assay that uses a specific *antigen* or *antibody*, capable of binding to the analyte, to identify and quantify substances. The antibody can be linked to a radioisotope [*radioimmunoassay (RIA*)] or to an enzyme that catalyzes an easily monitored reaction [*enzyme-linked immunosorbent assay (ELISA)*], or to a highly fluorescent compound by which the location of an antigen can be visualized (*immunofluorescence*).
[5]

immunoblot
Supporting substrate [often a nitrocellulose, nylon, or poly(vinylidene fluoride) membrane] onto which proteins that have been separated by gel electrophoresis are transferred and then identified by the binding of specific *antibodies*.
See also *immunoblotting*.

immunoblotting
western blotting
Technique for the detection, isolation, and quantitative measurement of specific immunoreactive polypeptides, separated into bands by polyacrylamide gel

electrophoresis, after which the bands are transferred from the gel to a membrane (*immunoblot*), followed by immunological detection of the immobilized *antigen* by the binding of specific *antibodies* typically labeled with peroxidase or radioactivity.

immunochemistry
Study of biochemical and molecular aspects of *immunology*, especially the nature of *antibodies*, *antigens*, and their interactions.
[5]

immunocompeten/ce (n), /**t** (adj)
Having the ability to exhibit an immune response.

immunocompromised
Unable to mount a full or effective *immune response*.

immunocytochemistry
See *immunohistochemistry*.

immunoconjugate
antibody conjugate
Antibody or antibody fragment to which a functional molecule, such as a drug, has been chemically linked.
See also *immunocytokine*.

immunocytokine
Antibody or antibody fragment to which a *cytokine* has been chemically linked.
Note: Such a construct may be used to direct a cytokine to its target cell.

immunodeficien/cy (n), /**t** (adj)
Inability to produce a normal repertoire of *antibodies* or immunologically sensitized *T lymphocytes*, especially in response to specific *antigens*.
Note 1: Defects in one or more components of the *immune system* result in the inability to eliminate or neutralize antigens.
Note 2: Congenital or primary immunodeficiencies are genetic or due to developmental disorders, such as congenital *thymic* aplasia (see also *thymic atrophy*).
Note 3: Acquired or secondary immunodeficiencies develop as a consequence of malnutrition, malignancies, *immunosuppressive* compounds, radiation or infection of *immunocompetent* T lymphocytes with *human immunodeficiency virus (HIV)*.
Note 4: Defects in *natural immunity* may also result in immunodeficiency.
Modified from [4]

immunodominant epitope
Epitope in an *antigen* that is preferentially recognized by *T cells*, which then come to dominate the *immune response*.

After [2]

immunodysregulation–polyendocrinopathy–enteropathy, X-linked
IPEX syndrome
X-linked syndrome characterized by immunodysregulation, polyendocrinopathy (*diabetes mellitus type 1*, *thyroiditis*), *hemolytic anemia*, *thrombocytopenia*, *dermatitis*, and enteropathy, caused by mutations in the gene encoding *Foxp3.*
[1]

immunoediting
Process of continuing *immunosuppression* of *immunogen*ic tumor cells, which may finally result in the selection of non-immunogenic tumor cells. It consists of the steps *immune elimination*, *immune equilibrium* and *immune escape*.

immunofluorescence
Technique for detection of cell- or tissue-associated *antigen*s by the use of a fluorescently tagged *ligand*, e.g., an anti-*immunoglobulin (Ig) conjugate*d to *fluorescein isothiocyanate (FITC)*.
[3]

immunogen
Any substance that elicits an *immune response*.
Note 1: Whilst all *immunogen*s are *antigen*s, not all antigens are immunogens.
See also *hapten*.
After [3, 4]

immunoglobulin (Ig)
Member of a glycoprotein family to which *antibodies* and *B-cell receptor*s *(BCR)* belong.
Note 1: Immunoglobulins bind to substances in the body that are recognized as foreign *antigen*s (often proteins on the surface of bacteria and viruses).
Note 2: Immunoglobulins also play a central role in *allergies* when they bind to antigens that are not otherwise a threat to health and provoke an inflammatory reaction.
See also *immunoglobulin*s *A, D*, *E, G,* and *M*.

immunoglobulin A (IgA)
Class of *immunoglobulin (Ig)* characterized by α *heavy chain*s.
Note: IgA antibodies are secreted mainly by *mucosa*l *lymphoid tissue*s, and in the dimeric form are present in mucosal secretions. IgA in the monomeric form is present in blood.
After [2]

immunoglobulin D (IgD)
Class of *immunoglobulin (Ig)* characterized by δ *heavy chain*s.
Note: It appears as a surface immunoglobulin on mature näive *B cell*s (see *näive*

lymphocyte) but its function is unknown.
After [2]

immunoglobulin E (IgE)
Class of *immunoglobulin (Ig)* characterized by ε *heavy chain*s.
Note: It is involved in the defense against parasite infections and in *allergic reaction*s.
After [2]

immunoglobulin Y (IgY)
Immunoglobulin (Ig) found in chickens.

immunoglobulin E (IgE)**-binding Fc receptors**
High-*affinity* IgE-binding *Fc*-ε-R type I *receptor*s are expressed on *mast cell*s and *basophil*s and interact with IgE *antibodies* with high affinity.
Note 1: The cross-linking of these receptors results in release of mediators such as *histamine*.
Note 2: The receptors are composed of α, β, and γ chains; the α chain contains the IgE binding site, while the γ chain is responsible for *signal transduction*.
Note 3: The low-affinity IgE binding *Fc receptor* (*CD23*) is expressed on *B cell*s, and its soluble (truncated) form is generated by proteolytic cleavage and regulates IgE production by B cells.
After [4]

immunoglobulin E (IgE)**-mediated hypersensitivity**
State in which an individual reacts with *allergic* effects caused fundamentally by the reaction of *antigen*-specific *immunoglobulin E (IgE)* following exposure to a certain substance (*allergen*) after having been exposed previously to the same substance.
[5]

immunoglobulin G (IgG)
Class of *immunoglobulin (Ig)* characterized by γ *heavy chain*s.
Note: It is the most abundant class of immunoglobulin found in the *plasma*.
After [2]

immunoglobulin M (IgM)
Class of *immunoglobulin (Ig)* characterized by μ *heavy chain*s.
Note 1: It is the first immunoglobulin to appear on the surface of *B cell*s and the first to be secreted.
After [2]
Note 2: Unlike other immunoglobulins that that exist in the monomeric (*IgA*, *IgD*, *IgE*, and *IgG*) or dimeric (*IgA*) state, IgM is found in the blood as a pentamer.

immunoglobulin gene superfamily
Genes encoding proteins containing one or more *immunoglobulin (Ig) domain*s

(homology units) that are homologous to either Ig *variable (V) region* or *constant (C) region* domains. Cell surface and soluble molecules mediating recognition, adhesion, or binding functions in and outside the *immune system*, derived from the same precursor, belong to this family of molecules (e.g., immunoglobulin, *T cell receptor (TCR)*, *major histocompatibility complex (MHC) class I* and *class II molecules*, *CD4*, *CD8*, and FcγR). [1]

immunoglobulin superfamily
Large family of proteins characterized by possession of 'immunoglobulin-type' domains of approximately 110 amino acids folded into two β-pleated sheets. Members include *immunoglobulin*s *A, E, G, M (IgA, IgE, IgG, and IgM)*, *T-cell receptor*s *(TCR)*, and *human leukocyte antigen (HLA) major histocompatibility complex (MHC) molecule*s.
See also *human leukocyte antigen (HLA)*, *immunoglobulin (Ig)*, *major histocompatibility complex (MHC) molecule*.
[3]

immunohistochemistry
Detection of cell-associated molecules in the light microscope with *antibodies* labeled with enzymes that change a substrate into a colored precipitate.

immunological ignorance
Absence of a pathogenic *autoimmune* response in spite of the concomitant presence in the *host* of the *autoantigen* and *T cell*s bearing the specific autoreactive *T-cell receptor (TCR)*.

immunological incompetence
Inability of the *immune system* to function in a normal fashion.

immunologically privileged site
Any of various sites in the body where foreign tissue *graft*s do not induce an immune reaction.

Note: Such sites include the eye, brain, testis, and unborn fetus. Although *antigen*s do migrate from these privileged sites, they either induce *immunological tolerance* or a nondestructive response.

immunological memory
immunological anamnesis
Ability of the *immune system* to respond faster and more effectively to subsequent exposures to an *antigen* following a *primary immune response* to the same antigen.

Note: Typically *memory T cell*s appear five days following initial immunization, whereas *memory B cell*s may take about a month to reach maximum levels. Populations of such cells may persist for the lifetime of the individual.

immunological synapse
Contact point between the *T-cell* and *antigen-presenting cell (APC)* that is generated by reorganization and clustering of cell surface molecules in *lipid raft*s. The synapse

facilitates interactions between *T-cell receptor (TCR)* and *major histocompatibility complkex (MHC) molecule*s, and between *adhesion molecule*s, thereby potentiating a TCR-mediated activation signal.
[3]

immunological tolerance
Persistent specific immunological unresponsiveness toward a substance that would normally be expected to elicit an *immune response*, resulting from previous non-sensitizing exposure to an *antigen*.

Note: Tolerance to specific foreign antigens can be induced by the exposure to the foreign antigens during embryonic or neonatal life (depending upon species). In adults, tolerance (usually of shorter duration) can be induced by using particular routes of administration for the antigens or administration of agents that are particularly effective against cells proliferating in response to antigen. Mechanisms may include deletion of potentially reactive *lymphocyte*s or their "inactivation" by immunological *suppression*.

Modified from [3, 20]

immunology
Science that deals with the *immune system* including *cell-mediated immunity (CMI)* and *humoral* aspects of *immunity* and *immune response*s.

immunomagnetic separation
Method of separating specific cell types or macromolecules with the aid of cell-specific *antibodies* coupled to paramagnetic beads.

immunomodulation
Modification of the functioning of the *immune system* by the action of a substance that increases or reduces the ability to produce an *immune response*.
After [5]

immunopathology
Study of diseases of the *immune system*. The occurrence of such diseases.

immunopathy
Disease of the *immune system*.
See also *immunopathology*.

immunopharmacology
1. Study of the *immune system* using drugs as diagnostic tools.
2. Use of pharmaceutical molecules to support and stimulate the immune system in patients with *immunodeficiency*, or to suppress or specifically influence the reactivity of the immune system in order to control a pathological immune reaction or disease.

immunophenotyping

Use of a panel of *antibodies* to determine a subset of proteins expressed on the surface of a cell or heterogeneous group of cells, often for diagnostic purposes, e.g., identifying the presence of *leukemia* cells in a population of *lymphocyte*s.

immunophilin
Any of a group of cytoplasmic proteins in *T cell*s that are targets of the *immunosuppressant* drugs cyclosporin A, tacrolimus (fujimycin), rapamycin, and related compounds.
See also Annex II for specific substances.

immunopotentiation
Enhancement of the capacity of the *immune system* to produce an effective response.
[5]

immunoprecipitate
Precipitate formed in an *antigen-antibody* reaction.

immunoprecipitation
Process of precipitating something by reaction with a specific *antibody* or *antigen*.

immunoreceptor tyrosine-based activation motif (ITAM)
Consensus sequence for src-family *tyrosine kinase*s, found in the cytoplasmic domains of several signaling molecules including the *signal transduction* units of *lymphocyte antigen receptor*s and of *Fc receptor*s.
[3]

immunoreceptor tyrosine-based inhibitory motif (ITIM)
Consensus sequence present in the cytoplasmic domains of certain cell surface molecules [e.g., Fc γ RIIB, inhibitory *natural killer (NK) cell receptor*s] and which mediates inhibitory signals.
[3]

immunosensitivity
Reactivity to *antigen*s.

immunosensitizer
Substance that makes the *immune system* more reactive to *antigen*s.

immunosorbent
Solid matrix on to which a specific *antibody* or *antigen* is adsorbed and used to capture the corresponding antigen or antibody from solution.

immunostimulating complex (ISCOM)
Immunological *adjuvant* composed of saponin, cholesterol, phospholipid, and an *immunogen*, usually protein.
Note: The adjuvant was originally designed to form a *vaccine* delivery system that

combined certain aspects of virus particles such as their size and orientation of surface proteins, with the powerful immunostimulatory activity of saponins.

After [23]

immunostimulation

Increase in immune function, e.g., by use of *bacille Calmette-Guérin (BCG) vaccine* or drugs.

Note: Immunostimulation may be beneficial (e.g., restoration of a depressed *immune response*) or detrimental (e.g., induction by drugs of *allergy, hypersensitivity*, or *autoimmunity*).

immunosuppressant

Substance that depresses the function of the *immune system*.

immunosuppression

Depression of the normal functioning of the *immune system*.

Note: This may be due to:

i. Inhibition of the normal response of the immune system to an *antigen*.

ii. Prevention, by chemical or biological means, of the production of an *antibody* to an antigen by inhibition of the processes of transcription, translation, or formation of tertiary structure.

After [5]

immunosuppressive

Causing depression of the normal function of the *immune system*.

immunosurveillance

Mechanisms by which the *immune system* is able to recognize and destroy malignant cells before the formation of an overt tumor.

[5]

immunotherapy

Treatment or prevention of a disease using agents that can modify the *immune response*.

Note 1: Immunotherapy is largely an experimental approach, applied most widely in the treatment of *leukemia*s, melanoma, and hypernephroma.

Note 2: Immunotherapy may involve *active* or *passive immunization*, *immunopotentiation* or *immunosuppression*, *hyposensitization*, *bone marrow transplantation*, or *thymus* implantation.

immunotoxic

Harmful to the *immune system*.

[5]

immunotoxicant

Substance that is harmful to the *immune system*.

immunotoxicology
Discipline applying cardinal principals of both *immunology* and toxicology to study the ability of certain substances to alter the *immune response*.

immunotoxin
Biochemical *conjugate*, or recombinant fusion protein, consisting of an immune targeting molecule such as an *antibody* or antibody fragment together with a *cytotoxic* molecule.
[3]
Compare *toxin*.

inactivated vaccine
Vaccine formulated from the whole microorganism that has been rendered unable to reproduce or cause disease, often by mutation or heat denaturation.
See also *attenuated vaccine*.

indirect antiglobulin test (IAT)
See *Coombs test*.

indirect Coombs test
See *Coombs test*.

indirect immunofluorescence
Method of visualizing an *antigen* in which an unlabeled *antibody* against the antigen is reacted with it first, and then is detected by staining with a second fluorescently tagged *immunoglobulin G (IgG)* directed against the first antibody.

indolamine-2,3-dioxygenase (IDO)
Enzyme catalyzing the initial rate-limiting step of *tryptophan* degradation.

Note 1: Tryptophan is required for *T cell* proliferation. Local degradation of tryptophan thus modulates T cell activity.

inducible co-stimulatory protein (ICOS)
Highly specific *receptor* for the protein B7H/B7RP-1 that is expressed on the surface of *B cell*s and *macrophage*s, and also appears on the surface of *T cell*s during the process of T-cell *activation*.

Note: Stimulation of the *B cell* and subsequent *antibody* production takes place after the ICOS *receptor* attaches to its partner B7RP-1 molecule. Thus, the co-stimulatory molecules, ICOS and B7H/B7RP-1, provide specificity for the *immune system* activation process.

infectious tolerance
Continuing state of *tolerance* that can be transferred by *T lymphocyte*s from a tolerant animal.

Note: Maintenance of *transplantation* tolerance involves the induction of *antigen*-specific *CD4+ regulatory T cell*s *(Treg)*.

After [24]

infertility, autoimmune

Infertility caused by sperm *antibodies*, *autoimmune* ovarian *inflammation* (oophoritis), or autoimmune orchitis.

Note: This disease may be part of a polyendocrinopathy.

[1]

inflammasome

High molecular weight complex that activates inflammatory *caspase*s and the *cytokines interleukin*-1β (IL-1β) and IL-18.

Note: There appear to be at least three types of inflammasomes. Those identified initially were the NALP1 inflammasome, the *NALP3* (*cryopyrin*) inflammasome, and the *interleukin- (IL-)*1 β converting enzyme (ICE) protease activating factor (IPAF) inflammasome.

[25]

See also *inflammation*.

inflammation

Reaction of the body to injury or to infectious, *allergic*, or chemical irritation; characterized by redness, swelling, heat, and pain resulting from dilation of the blood vessels accompanied by loss of *plasma* and *leucocyte*s into the tissues.

[5]

inflammatory bowel disease (IBD)

Group of chronic inflammatory conditions resulting in the inappropriate and persistent activation of the *mucosa*l *immune system* of the bowel.

Note 1: Idiopathic IBD is a set of chronic conditions probably driven by the presence of normal intestinal flora.

Note 2: Autoantibodies against proteins of *neutrophil granulocyte*s, pancreatic acinus, intestinal goblet, and colonic epithelial cells are detectable.

Note 3: Crohn disease and ulcerative colitis are two variants of IBD with overlapping clinical manifestations and probable *autoimmune* origins. Crohn disease is immunologically characterized by antibody to Saccharomyces cerevisia*e* and *Th1 cell*-dominated responses.

After [1, 19]

inflammatory response

See *inflammation*.

innate immunity

Immunity that is not intrinsically affected by prior contact with *antigen*, i.e., all aspects of immunity not directly mediated by *lymphocyte*s.

[3]

insulin-dependent diabetes mellitus (IDDM)
See *diabetes mellitus type 1*.

integrin
Member of a family of heterodimeric *adhesion molecule*s, mediating attachment of the cell to other cells or to the extracellular matrix, and thereby signaling information to the cell about its surroundings.

intercellular adhesion molecule (ICAM)
Member of the *immunoglobulin superfamily* that interacts with *integrin*s and is found on the surface of several cell types, including *antigen-presenting cell*s *(APC)* and *T cell*s.

interclonal competition
Process which favors survival of foreign-specific *lymphocyte*s at the expense of self-specific lymphocytes and is a secondary mechanism involved in the induction and maintenance of *self-tolerance*.
After [1]

interdigitating dendritic cell
See *dendritic cell*.

interferon (IFN)
Any of a group of glycoproteins that are produced by cells in response to stimuli, such as exposure to a virus, bacterium, parasite, or other *antigen*, and that prevent viral replication in newly infected cells and, in some cases, modulate specific cellular functions.

Note 1: There are three classes: α, β, and γ. Alpha interferon (IFN-α) is made by *lymphocyte*s and *macrophage*s. Beta interferon (IFN-β) is synthesized by *fibroblast*s and epithelial cells. Alpha and beta interferons were once called type 1 interferon. Gamma interferon [see *γ-interferon (IFN-γ)*], also called type 2 interferon, is synthesized by lymphocytes.

Note 2: All three interferon classes can be induced during viral infection. They have antiviral and antiproliferative effects, and all induce expression of *major histocornpatibility complex (MHC) class I molecule*s.

interleukin (IL)
Member of a group of immunoregulatory glycoproteins, also called *lymphokine*s, *monokine*s, or *cytokine*s.

Note 1: General features are low relative molecular mass (about 80 kDa) and frequent glycosylation; regulation of immune cell function and *inflammation* by binding to specific cell surface *receptor*s; transient and local production; action in *paracrine*, *autocrine*, or endocrine manner, with stimulatory or blocking effect on growth/differentiation; very potent, function at picomolar concentrations.

Note 2: Interleukins represent an extensive series of mediators with a wide range

of overlapping functions. Other mediators in this series are c-kit *ligand*, *interferon*s *(IFN)*, *tumor necrosis factor (TNF)*, *transforming growth factor* β *(TGF-*β*)*, and a family of low relative molecular mass mediators, called *chemokine*s.

Modified from [4]

internal image
Epitope on an anti-*idiotype* that binds in a way that structurally and functionally mimics the *antigen*.
[3]

intolerance (in immunology)
Extreme sensitivity or *allergy* to a drug, food, or other substance.

intradermal test
Diagnostic test for a possible cause of *hypersensitivity* in an individual in which a small drop of *antigen* is placed on a scarified skin surface or injected intradermally.

Note: Production of an *immune response* in the treated skin represents a positive result.

intra-epithelial lymphocyte (IEL)
Lymphocyte found in the epithelial layer of mammalian *mucosa*l linings, such as those of the gastrointestinal and reproductive tracts.

intrinsic pathway (of apoptosis)
Pathway of cell death initiated from within the cell, usually in response to signals following DNA damage, a defective cell cycle, detachment from the extracellular matrix, hypoxia, loss of cell survival factors, or other types of severe cell stress.

Note: This pathway involves the release of pro-*apoptotic* proteins from the mitochondria.

See also *apoptosis*, *extrinsic pathway (of apoptosis)*.

invariant chain
CD74
Protein (31 kDa) of the endoplasmic reticulum lumen that binds to newly formed *major histocompatibility complex (MHC)* heterodimeric proteins, preventing binding of endogenous peptides to their groove.

Note: This protein acts as a chaperone for these molecules until they leave the Golgi apparatus and enter the *endosome* pathway. It is degraded proteolytically but leaves a fragment (called CLIP) bound within the groove of the *major histocompatibility complex (MHC) class III molecule*s. In acid vesicles, after leaving the Golgi apparatus, CLIP exchanges with peptides derived from exogenous *antigen*s.

IPEX syndrome
See *immunodysregulation–polyendocrinopathy–enteropathy, X-linked*.

ir genes
See *immune response genes*.

islet cell antibodies (ICA)
Autoantibodies reacting with endocrine (pancreatic islet) cells and detectable by *indirect immunofluorescence* on pancreatic cryostat sections.
Note: Islet cell antibodies are diagnostic markers of *diabetes mellitus type 1*.

isoantigen
See *alloantigen*.

isograft
syngraft
Tissue *transplant*ed (see *graft*) between two genetically identical individuals.

isohemagglutinin
Naturally occurring *imunoglobulin M (IgM) antibody* specific for the *erythrocyte antigen*s of the *ABO blood group*s, thought to result from *immunization* by bacteria in the gastrointestinal and respiratory tracts.
After [7]

isotype
Class of *antibody* that differs from others in the *constant region* of the *heavy chain* (*Fc* portion).

isotype control
Antibody exhibiting the non-specific characteristics of the antibody-*isotype* but lacking any specificity for the *antigen* in question; used as a negative control in antibody-antigen detection assays, notably in *flow cytometry*.

isotype switch
Process by which a *B cell* switches from making *antibody* of one *isotype* to another without altering the specificity of the antibody, producing an isotype with the same *variable (V) region*s but a different *heavy chain constant (C) region*.

J chain
See *joining (J) chain*.

J gene
See *joining (J) gene*.

JAK/STAT signaling pathway
Mechanism that transmits information from chemical signals outside the cell to gene promoters on the DNA in the cell nucleus. The mechanism is activated by the binding of *Janus-family tyrosine kinase (JAK)* to the nonpolypeptide portion of occupied

*receptor*s for some *interleukin*s *(IL)*. JAK phosphorylates signal transducer and activator of transcription (STAT) proteins apart from STAT 5a and 5b.

Note: JAK2 is activated after it binds occupied receptors for somatotropin, several *cytokine*s, and leptin. It then phosphorylates STAT proteins, which dimerize and enter the nucleus to activate transcription of specific genes.

JAM test
Method which uses labeled nucleotide precursors to estimate DNA fragmentation during *cell-mediated cytotoxicity* or *apoptosis*.

Janus-family tyrosine kinase (JAK)
Tyrosine kinase activated by *cytokine*s binding to cell *receptor*s.
See also *JAK/STAT signaling pathway*.

Jerne plaque assay
See *antibody-forming cell (AFC) assay*.

joining (J) chain
Polypeptide that forms part of the polymeric structure of pentameric *immunoglobulin M (IgM)* and dimeric *immunoglobulin A (IgA)*.
After [3]

joining (J) gene
Gene coding for a joining segment that connects *variable (V) region*s and c*onstant (C) region*s of *immunoglobulin (Ig)* or *T-cell receptor (TCR)* chains that, upon gene rearrangement, encodes part of the third *hypervariable region* of the *antigen receptor*s.

Note: In Ig *light chain*s and TCR, a *variable (V) gene* segment rearranges to a *joining (J) gene* segment; in Ig *heavy chain*s and TCR, a *diversity (D) gene* segment rearranges to a joining (J) gene segment.

See also *V(D)J recombination*.
Modified from [3, 7]

junctional diversity
Diversity of the splice junctions in the recombined *variable (V) gene*, *diversity (D) gene* [for *immunoglobulin (Ig) heavy chain*s, and for TCR b and d chains], and *joining (J) gene* segments of *antibody* and *T-cell receptor (TCR)* genes.
See also *D gene* and *V gene*.
[3]

K cell
See *killer cell*.

kallikrein
Any of a group of enzymes found in the blood and body fluids that acts on certain *plasma globulin*s to produce *bradykinin*s.

Kaposi sarcoma (KS)
Form of skin cancer that can involve internal organs. It is most often found in patients with *acquired immunodeficiency syndrome (AIDS)* and can be fatal.

kappa (κ)-light chain
Smaller of the two types of *light chain* found in human *immunoglobulin*s *(Ig)*, the other type being a *lambda (λ)-light chain*.
See also *Bence Jones protein*.

keratinocyte
Epidermal cell that produces keratin.

killer activatory receptor (KAR)
killer cell immunoglobulin-like receptor
Receptor found on *natural killer (NK) cell*s, and some $\gamma{:}\delta$ and $\alpha{:}\beta$ *T cell*s.
Note 1: KARs recognize *major histocompatibility complex (MHC) class I molecule*s and, like the *C-type lectin* receptors also found in these cells, can either inhibit or activate the *killer cell*s. If *immunoreceptor tyrosine-based inhibitory motif (ITIM)* sequences are present in their cytoplasmic domain they are inhibitory.
*Note 2: Killer cell immunoglobulin-like receptor*s *(KIR)* lacking ITIMs can associate with *immunoreceptor tyrosine-based activation motif (ITAM)*-containing adaptor molecules in which case they can activate the killer cell.
[26]

killer cell
Cell that displays *cell-mediated cytotoxicity*, including *cytotoxic T lymphocyte*s *(CTL, Tc)*, *natural killer (NK) cell*s, and *natural killer T (NKT) cell*s. Some also consider activated *macrophage*s, *monocyte*s, and *interferon (IFN)*-activated *neutrophil*s to be killer cells.

killer cell immunoglobulin-like receptor (KIR)
killer inhibitory receptor
Receptor expressed on *natural killer (NK) cell*s that binds to *major histocompatibility complex (MHC) class I molecule*s on *target cell*s; binding MHC class I inhibits the signaling that would otherwise lead to target cell killing.
Note: If *immunoreceptor tyrosine-based inhibitory motif (ITIM)* sequences are present in the KIR cytoplasmic domain, MHC class I molecule binding is inhibitory to the *killer cell*. KIRs lacking ITIMs can associate with *immunoreceptor tyrosine-based activation motif (ITAM)*-containing adaptor molecules, in which case binding of MHC class I molecules can activate the killer cell.

killer lectin-like receptor (KLR)
Killer cell receptor that binds to *major histocompatibility complex (MHC) class I molecule*s and, like the *C-type lectin* receptors also found on these cells, can either inhibit or activate the killer cells.

killer T cell
See *cytotoxic T lymphocyte*.

kinin
Any of a family of polypeptides that is released during inflammatory responses and that increases vascular permeability and smooth muscle contraction.
After [3]

knockout
Use of homologous genetic recombination in embryonic *stem cell*s to replace a functional gene with a defective copy of the gene.
Note: The animals that are produced by this technique can be bred to homozygosity, thus allowing the generation of a null phenotype for that gene product.
[3]
See also *knockout mouse*.

knockout mouse
Mouse produced from embryonic cells containing DNA that has been genetically engineered so that it does not express a particular gene or group of genes.

Kupffer cell
Fixed tissue *macrophage* found lining the blood sinuses in the liver.
After [3]
See also *macrophage, resident(ial).*

Kviem reaction
Test for *sarcoidosis*, eliciting a *granuloma* at the site of intrradermal injection of a *lymph node* extract from a person with active disease. Generally considered non-specific.

L-selectin
Any of a group of *leukocyte* surface *adhesion molecule*s; they are classed as CD62 in the *cluster of differentiation (CD) antigen* marker system. All have *lectin* family carbohydrate binding domains and epidermal growth factor (EGF) repeats.
Note: L-selectins are expressed on the surface of *platelet*s and endothelial cells as well as leukocytes.
[26]

Ly-6
Family of multi-gene-encoded, small, generally glycosylphosphatidyl inositol-anchored membrane proteins thought to be involved in cell adhesion and signaling, and in *antigen*-independent *activation* of *lymphocyte*s.
See also *protectin (CD59)*.

Lambert-Eaton myasthenic syndrome (LEMS)

Paraneoplastic (see *paraneoplastic autoimmune syndrome*) neurological disorder associated with small-cell lung cancer and caused by *autoantibodies* against voltage-gated calcium channels.
[1]

lamda (λ)-light chain
One of the two types of *light chain* of human *immunoglobulin*s *(Ig)*, the other type being the *kappa (κ)-light chain*.

Langerhans cell
Immature, phagocytic *dendritic cell* of the mammalian skin, characterized by the presence of *Fc receptor*s, *major histocompatibility (MHC) class II molecule*s, and epidermal dendritic cell marker *CD1*. It contains a cytoplasmic organelle called the Birbeck granule.

large granular lymphocyte (LGL)
Lymphocyte of greater than normal size that contains cytoplasmic granules and functions as a *natural killer (NK) cell* or *killer (K) cell*. Activated *CD8+ cytotoxic T lymphocytes (CTL, Tc)* also assume an LGL morphology.
After [3]

late phase reaction
Immunoglobulin E (IgE)-mediated immune response occurring 5 to 8 hours after exposure to *antigen*, after the '*wheal* and flare' reaction of immediate *hypersensitivity* has diminished, with *inflammation* peaking around 24 hours, and then subsiding.

latex agglutination test
latex fixation test
Use of latex beads coated with *antibodies* to detect *antigen* in biological samples.

latex allergen
Allergen found in natural rubber latex (NRL).
Note: Major NRL-specific allergens are Hev b 1, Hev b 3, Hev b 5 and Hev b 6.02. These four major allergens account for the allergenic potential of NRL products like gloves, condoms, teats, balloons, etc.

lectin
Member of a family of proteins that binds specific sugars on glycoproteins and glycolipids. Some plant lectins are *mitogenic* [e.g., *phytohemagglutinin (PHA)*, *concanavalin A (ConA)*].
[3]

leukemia
Progressive, malignant disease of the blood-forming organs, characterized by excessive proliferation and development of *leucocyte*s and their precursors in the *bone marrow* and blood.

[5]

leukocyte
White blood cell.
Note: There are different types of leukocyte including *neutrophil*s, *basophil*s, *eosinophil*s, *lymphocyte*s and *monocyte*s.
After [3]

leukocyte common antigen (LCA)
Antigen common to both *T lymphocyte*s and *B lymphocyte*s.

leukocyte functional antigen (LFA)
Any of a group of cell-surface *antigen*s involved in intercellular adhesion.

leukocytopenia
Amount of *leukocyte*s below normal values that is a characteristic feature of *systemic autoimmune disease*s [e.g., Felty syndrome, *systemic lupus erythematosus (SLE)*, *Sjögren syndrome, mixed connective tissue disease (MCTD)*].
After [1]

leukocytosis
Abnormal increase in the number of *leukocyte*s.
[1]

leukopenia
See *leukocytopenia*.

leukotriene
Metabolic product of arachidonic acid that promotes inflammatory processes (e.g., *chemotaxis*, increased vascular permeability) and is produced by a variety of cell types including *mast cell*s, *basophil*s and *macrophage*s.
[3]

ligand
Ion, molecule, or molecular group that binds to another chemical entity to form a larger complex.
[5]
Note: A ligand may bind specifically to a *receptor* and trigger a response such as activation of a *signal transduction* pathway.

ligand of inducible co-stimulatory protein (ICOSL, LICOS)
Protein involved, after binding to *inducible co-stimulatory protein (ICOS)*, in several harmful *immune response*s, such as *autoimmunity*, *allergy*, or *graft-versus-host (GVH) reaction*.
Note: Prolonged ICOS and ICOSL expression at chronic inflammatory sites seems to give rise to pathology.

light chain
Small polypeptide subunit of an *antibody* or *immunoglobulin (Ig*).
Note: A typical antibody is composed of two immunoglobulin (Ig) *heavy chain*s and two Ig light chains.

limulus test
Method of detecting bacterial *endotoxin*s based on gelation of a blod cell lysate from the horseshow crab.
See also *pyogen test*.

linear epitope
continuous epitope
Antigenic determinant that is contiguous in the amino acid sequence of a protein and therefore does not require the protein to be folded into its native conformation for *antibody* to bind.
Note: The *epitope*s detected by *T cell*s are continuous.
After [2]

linked recognition
Requirement for a *helper T lymphocyte (Th)* and *B lymphocyte* to interact with separate but physically linked *epitope*s in the same *antigen*, in order for an *immune response* to a *thymus-dependent (TD) antigen*.

lipid raft
Cholesterol- and glycosphingolipid-rich membrane subdomain in which molecules involved in cellular *activation* become concentrated.
[3]
See also *caveola*.

lipopolysaccharide (LPS)
Endotoxin derived from Gram-negative bacterial cell walls, which has inflammatory and *mitogenic* actions.
[3]

live attenuated vaccine
Vaccine prepared from living attenuated organisms or from viruses that have been attenuated but can still replicate in the cells of the *host* organism.
Note: The live attenuated vaccine contains a version of living bacteria or viruses that have been weakened (attenuated) so they can no longer cause disease. Since they are very close to the actual infection, they can cause strong cell and *antibody* responses.
See also *attenuated vaccine*.

liver–kidney microsomal antibodies (LKM)
Autoantibodies directed against cytochrome P450 and uridine diphosphate (UDP)-

glucuronosyltransferase (UGT) *antigen*s typically found in patients with immune-mediated hepatitis.

Note: These include LKM-1 *antibodies* (cytochrome P4502D6) in patients with *autoimmune* hepatitis type 2 (AIH-2) and *autoimmunity* associated with hepatitis C; LKM-2 (cytochrome P4502C9) in patients with drug-induced hepatitis caused by tienilic acid; and LKM-3 (UGT-1) in patients with chronic hepatitis D and AIH-2.

[1]

local lymph node assay (LLNA)
See *murine local lymph node assay (LLNA)*.

lupus
See *systemic lupus erythematosus (SLE)*.

lupus anticoagulant
See *anticoagulant, lupus*.

lupus erythematosus
See *systemic lupus erythematosus (SLE)*.

lupus-like syndrome
See *drug-induced lupus*.

lymph
Clear fluid that bathes the tissues of the body, carrying bacteria to *lymph node*s and ultimately to the blood stream.

Note 1: Lymph can also transport metastatic cancer cells.

Note 2: Lymph plays a role in maintaining body fluid balance.

See also *lymphatic (system)*.

lymphadenopathy
Enlarged *lymph node*s.
[3]

lymphangion
Morphological or functional unit of *lymphatic* vessels consisting of the region between adjacent lymphatic valves.

lymphatic (system)
Describing vessels whose special function is the collection of *lymph* and its ultimate conveyance to the blood circulation and thoracic duct.

lymphatic tissue
Tissue involved in the collection, production, and handling of *lymph*, including the lymphatic vessels and *lymph node*s.

lymph node
lymph gland
Any of the small rounded gland-like structures of the *lymphatic system*, which occur along the lymphatic vessels and which are responsible for removing bacteria, viruses and foreign molecules from the *lymph* stream and for producing *lymphocyte*s and *antibodies*.

lymphoblast (n**), /ic (**adj)
Abnormal cell with a large nucleus and scanty cytoplasm, thought to be the precursor of the *lymphocyte*, found in blood and blood-forming organs in patients with lymphoblastic *leukemia*.

lymphocyte
Any small *leucocyte* found in the blood, *lymph*, and *lymphoid tissue*s that has a single round nucleus and little or no granulation in the cytoplasm; lymphocytes may be either *B cell*s, which produce *humoral immunity*, or *T cell*s, which produce *cell-mediated immunity (CMI)*.

Note: Lymphocytes constitute about a quarter of the total leucocytes in the blood stream but occur in large numbers in the *lymph node*s and other *lymphatic tissue*.

lymphocyte-activated killer cell
See *lymphokine-activated killer cell (LAK)*.

lymphocyte-activating factor
Interleukin-1 (IL-1)
See *interleukin (IL)*.

lymphocyte activation
Sum of the biochemical processes necessary to stimulate a resting *lymphocyte* to become an immune effector cell, requiring *antigen* and costimulatory molecules.

lymphocyte blastogenesis assay (LBA)
See *lymphocyte transformation test (LTT)*.

lymphocyte function-associated antigen-1 (LFA-1)
Adhesion molecule found on *lymphocyte*s, *macrophage*s, and *neutrophil*s, involved in adhesion of lymphocytes to *antigen-presenting cell*s *(APC)*.

lymphocyte homing
Process that directs *lymphocyte* subsets to specialized microenvironments that control their differentiation, regulate their survival, and target immune effector cells to sites of *antigenic* or microbial invasion.
See also *homing*, *homing receptor*.

lymphocyte homing receptor
Cell surface glycoprotein on *lymphocyte*s and other *leukocyte*s that mediates adhesion to specialized blood vessels, the *high endothelial venules*.

Note: Several different classes of lymphocyte homing receptors have been identified, and they appear to bind to different surface molecules (*addressins*) on high endothelial venules in different tissues.

lymphocyte proliferation test (LPT)
Test of immune *sensitization* in which white blood cells are exposed in vitro to an *antigen* and multiply if already sensitized to that antigen.
See also *lymphocyte transformation test (LTT)*.

lymphocyte repertoire, immunoglobulin or T-cell receptor
Profile of *immunoglobulin*s *(Ig)* or *T-cell receptors (TCR)* available within a specified group of cells.

Note: Each profile is characterized by the *antigen* specificities of the immunoglobulins or T-cell receptors present.

lymphocyte subpopulation
Population forming part of the whole population of *lymphocyte*s, usually characterized by sensitivity to a given *antigen*.

lymphocyte transformation test (LTT)
lymphocyte blastogenesis assay (LBA)
Test for increased DNA synthesis followed by cell division and differentiation of *lymphocyte*s in response to *antigen*s or *mitogen*s; an in vitro test of lymphocyte function.
See also *lymphocyte proliferation test*.

lymphocytopenia
Deficiency of *lymphocyte*s in the blood compared with normal values.

Note: This is a characteristic feature of *systemic autoimmune disease*s [e.g., *systemic lupus erythematosus (SLE)*, *Sjögren syndrome*, *mixed connective tissue disease (MCTD)*].

After [1]

lymphocytosis
Condition characterised by an abnormal increase in the number of *lymphocyte*s in blood, usually a result of infection or inflammation.

lymphocytotoxicity
Capability of lysing *lymphocyte*s.

Note: Lymphocytes having a specific cell surface *antigen* are lysed when incubated with *antiserum* and *complement* or when attacked by *primed histoincompatible T lymphocyte*s.

lymphoid follicle

Region of clustered *B cell*s, allowing the selection of *antigen*-binding B cells by *dendritic cell*s during *adaptive immune response*s.

lymphoid stem cell
Stem cell giving rise to the lineage of *lymphocyte*s.

lymphoid tissue
Any vertebrate tissue that is made up predominantly of *lymphocyte*s, e.g. *lymph*, *lymph node*s, *spleen*, *thymus*, *Peyer's patch*es, adenoids, pharyngeal *tonsil*s, and, in birds, *bursa of Fabricius* and cecal tonsils.
[26]

lymphokine
Cytokine produced by *lymphocyte*s.
[3]

lymphokine-activated killer cell (LAK)
lymphocyte-activated killer cell
Killer (K) cell or *natural killer (NK) cell* activated *in vitro* by *interleukin (IL)*-2 to give enhanced killing of *target cell*s.
[3]

lymphoma
Any neoplasm, usually malignant, of the *lymphatic tissue*s.

lymphopenia
See *lymphocytopenia*.

lymphopoiesis
Production of *lymphocyte*s.

lymphoproliferation
Proliferation of *lymphocyte*s in response to stimulation with cellular activators, including *antigen*s or *mitogen*s.

lymphosum
Sum of *B cell*s + *T cell*s + *natural killer (NK) cell*s determined separately (by *flow cytometry*), compared to the total number of *lymphocyte*s.

Note: Used as a check on accuracy in counting the proportion of cell types, e.g., a value of (100 ± 10)% being acceptable and reflecting the uncertainty of the method.

lymphotoxin (LT)
Tumor necrosis factor β (TNF-β)
T cell-derived *cytokine* that is *cytotoxic* for certain tumor cells and also has immunoregulatory functions.

[3]

lysosome
Cytoplasmic granule containing hydrolytic enzymes involved in the digestion of phagocytosed (see *phagocytosis*) material.
After [3]

M cell
See *microfold cell*.

macroautophagy
non-specific autophagy
Sequestration and breakdown of organelles and long-lived proteins in a double-membrane vesicle, called an autophagosome or autophagic vacuole, inside the cell.

Note 1: The outer membrane of the autophagosome fuses in the cytoplasm with a *lysosome* to form an autolysosome or auto*phagolysosome* where their contents are degraded by acidic lysosomal hydrolases.

Note 2: Macroautophagy is the major inducible pathway for the general turnover of cytoplasmic constituents in eukaryotic cells. It is also responsible for the degradation of active cytoplasmic enzymes and organelles during nutrient starvation.

See also *autophagy*.

macrophage
Large (10–20 μm diameter) ameboid and phagocytic cell (see *phagocyte*) found in many tissues, especially in areas of *inflammation*, derived from blood *monocyte*s and playing an important role in *host defense* mechanisms.
[5]

Note: Two main functions are recognized: *phagocytosis* and *antigen presentation*.

macrophage, resident(ial)
macrophage, fixed
Macrophage stationed at a point where microbial invasion or accumulation of dust is likely to occur.

Note: Each type of macrophage, determined by its location, has a specific name:

Name of cell	Location
Dust cells/alveolar macrophages	pulmonary alveolus of lungs
Histiocytes	connective tissue
*Kupffer cell*s	liver
Microglial cells	neural tissue
*Monocyte*s	blood
Osteoclasts	bone
Sinusoidal lining cells	*spleen*

macrophage function test

Any assay suitable to characterize the effect of substances on *macrophage* function in vivo or in vitro.

Note: Common macrophage function tests are the *chromium release assay* and the *chromate uptake assay*.

macrophage mannose receptor (MMR)
Receptor involved in pathogen recognition, in clearance of endogenous serum glycoproteins, and in *antigen presentation*.

Note 1: Clusters of lectin domains bind mannose residues on microbial and fungal surfaces in a Ca^{2+}-dependent manner.

Note 2: The receptor activates the C3 component of *complement*.

macropinocytosis
'High-volume' *pinocytosis* by which *dendritic cell*s engulf relatively large volumes of fluid from their surroundings, enabling them to take in many *antigen*s nonspecifically.

major basic protein
Small basic arginine-rich peptide (pI 10.9, relative molecular mass of 13.8 kDa) in the granules of *eosinophil*s that kills helminths and protozoa.
[4]

major histocompatibility complex (MHC)
Cluster of genes encoding cell surface molecules involved in *antigen presentation* to *T cell*s. In humans, they are found on chromosome 6 and in mice on chromosome 17. They are polymorphic and code for *antigen*s that lead to rapid *graft rejection* between members of a single species that differ at these loci.

Note: Several classes of protein such as *MHC class I* and *II molecules* are gene products encoded in this region. The MHC-encoded molecules are also known as *human leukocyte antigen*s *(HLA)*.

See also *H-2*, *H-2 complex*.

major histocompatibility complex (MHC) **class I molecule**
Surface protein encoded by the *major histocompatibility complex (MHC)* expressed on all nucleated cells, presenting antigen-derived peptides.
See also *antigen presentation*.
After [1]

major histocompatibility complex (MHC) **class II molecule**
Surface protein encoded by the *major histocompatibility complex (MHC)* expressed on *antigen-presenting cell*s *(APC)*, presenting antigen-derived peptides.
See also *antigen presentation*.
After [1]

major histocompatibility complex (MHC) **class III molecule**
Antigen encoded by the *major histocompatibility complex (MHC)* including several *complement* factors, *tumor necrosis factor (TNF)* α, and *lymphotoxin*.

Note: The genes are found on the short arm of chromosome 6 between class I and class II genes, and although the gene products share no common function with the *major histocompatibility complex (MHC) class I* and *MHC class II molecules*, they are often discussed together.

major histocompatibility complex (MHC) **molecule**
Any of the cell-surface glycoprotein *alloantigens* encoded by the *major histocompatibility complex (MHC)* that are involved in the regulation of *immune response*s and can cause the *rejection* of *graft*ed tissues, cells, and tumors bearing them.

major histocompatibility complex (MHC) **restriction**
Necessity that *T cell*s recognize processed *antigen* only when presented by *major histocompatibility complex (MHC) molecule*s of the original *haplotype* associated with T-cell *priming*.
[3]

Mancini immunodiffusion
See *radial immunodiffusion*.

mammalian target of rapamycin (mTOR)
Intracellular signaling molecule (phosphoinositide-3-kinase) involved in control of cell growth, whose activity is negatively influenced by the *immunosuppressive* drug rapamycin (Annex II).

mannan-binding lectin-associated serine peptidase-1 and -2 (MASP1, MASP2)
mannose-binding protein-associated serine protease (MASP)
Complement-dependent bactericidal factors that bind to the Ra and R2 polysaccharides expressed by certain enterobacterium strains, such as Ra *chemotype* strains of Salmonella.

Note 1: Alternate splicing of the genes results in multiple transcript variants encoding two Ra-reactive factors (RARF) that are involved in the *mannose-binding lectin (MBL)* pathway of complement activation.

Note 2: They are serine proteases that share about 40% sequence identity with complement components C1r and C1s.

mannose-binding lectin (MBL)
mannan-binding lectin
See *mannose-binding protein*.

mannose-binding protein (MBP)
mannose-binding lectin (MBL)
Member of the *collectin* family of calcium-dependent *lectin*s, and an *acute phase protein*.

Note: This lectin functions as a stimulator of the *classical pathway of complement activation*, and as an *opsonin* for *phagocytosis* by binding to mannose, a sugar residue usually found in an exposed form only on the surface of

microorganisms.
[3]

mantle zone
mantle
corona
Outer ring of small *lymphocyte*s surrounding the centre of a lymphatic nodule (*lymphoid follicle*). It contains transient lymphocytes and is the location of the *lymphoma* in mantle cell lymphoma.

Mantoux test
See *tuberculin*.

marginal zone
Outer area of the *splenic* periarteriolar lymphoid sheath (PALS) that is rich in *B cell*s, particularly those responding to *thymus*-independent *antigen*s.
[3]

margination
Leukocyte adhesion to the endothelium of blood vessels in the early phase of an acute *inflammatory response*.
[3]

marrow, bone
Soft fatty vascular substance in the cavity of bone where blood cells are formed.

mast cell
Large connective tissue cell that contains inflammatory substances such as *histamine*, proteases (including tryptases, chymases, and carboxypeptidase A), heparin and chondroitin sulfate proteoglycans, and eicosanoid lipid mediators (the precursors of *leukotriene*s and *prostaglandin*s). These substances are released in *allergic* reactions or in response to injury or *inflammation*.

Note: Mast cells are bound within tissues that interface with the external world such as the skin, respiratory or intestinal tract, as well as in other areas such as heart, synovium, and uterus. Mast cells do not circulate. The mast cell has binding sites on its surface for *immunoglobulin E (IgE)*.

mast cell activation disorder (syndrome) (MCAD/MCAS)
Disorder or syndrome in which there is evidence of *systemic*, inappropriate release of *mast cell* mediators.

Note: While people with MCAD/MCAS have a normal or near-normal tryptase level and a *bone marrow* biopsy that contains a normal number of mast cells, they experience most of the same symptoms as someone with *mastocytosis*.

mast cell degranulation

See *degranulation*.

mast cell stabilizer
Non-steroidal medication that reduces the release of substances from *mast cell*s, e.g., sodium cromoglycate.

mastocyte
See *mast cell*.

mastocytoma
mast cell tumor
Nodule of *mast cell*s that can involve the skin, subcutaneous tissue, and sometimes muscle.

Note: Mastocytomas are rare and are mostly seen in infants within the first 3 months of life.

mastocytosis
Rare disease characterized by the presence of too many *mast cell*s in various organs and tissues. The condition can be a chronic, long-term illness or it can develop suddenly.

Note: Mastocytosis may be *systemic*, involving a variety of organs, or cutaneous, involving only the skin, also referred to as urticaria pigmentosa.

maturation (in immunology)
Process by which *B cell*s produce *antibodies* with increased *affinity* for *antigen* during the course of an *immune response*.

mature B cell
B cell with *immunoglobulin M (IgM)* and *immunoglobuling D (IgD)* on its surface.

medulla
Inner (central) region of an organ.
[3]

megakaryocyte
Bone marrow precursor of *platelet*s.
[3]

membrane attack complex (MAC)
Complex of *complement* components C5b–C9 that inserts as a pore into the membrane of *target cell*s leading to cell lysis.
[3]

memory (in immunology)
immunological memory
Characteristic of the acquired *immune response* (see *acquired immunity*) of

*lymphocyte*s whereby a second encounter with a given *antigen* produces a secondary immune response that is faster, greater and longer lasting than the *primary immune response*.
[3]

memory cell
Clonally expanded *T cell* or *B cell* produced during a *primary immune response* and which is *prime*d to mediate a *secondary immune response* to the original *antigen*.
[3]

memory lymphocyte immunostimulation assay (MELISA)
Patented modification of the *lymphocyte transformation test (LTT)* based on the *enzyme-linked immunosorbent assay (ELISA)* principle.

mesenteric lymph node
Lymph node lying between layers of the mesentery.

metabolic activation
Formation of one or more chemically reactive intermediate(s) as a result of modification of a molecule by the *xenobiotic*-metabolizing enzymes of liver and other organs.

Note1: This may lead to acute cell damage and recognition of the damaged cell by the *immune system* as *non-self*.

Note 2: The reactive intermediate can also act as a hapten.

microautophagy
Process in which *lysosome*s directly engulf cytoplasm by invagination, protrusion, and (or) septation of the lysosomal limiting membrane.
See also *autophagy*.

microfold cell
M cell
Cell found in the follicle-associated epithelium of the *Peyer's patch* that has the unique ability to sample *antigen* from the lumen of the small intestine and deliver it via *transcytosis* to *antigen presenting cell*s *(APC)* and *lymphocyte*s located in a unique pocket-like structure on their basolateral side.

microglobulin
Any small globular protein found on the surface of many cells, including *lymphocyte*s, and in the blood *plasma* distinct from albumin.

microscopic polyangiitis (MPA)
ANCA-associated necrotizing, *pauci-immune vasculitis* of the small vessels (capillaries,venules, arterioles) frequently associated with rapidly progressive *glomerulonephritis* and (or) hemorrhagic *alveolitis* as well as *autoantibodies* against *myeloperoxidase*.
[1]

migration (of cells)
Movement of cells from one part of the developing embryo or the body to another part.
Note: Cells often migrate in response to, and towards or away from, specific external signals, a process called *chemotaxis*.

minor histocompatibility antigen
Non-*major histocompatibility complex (MHC)*-encoded cell surface processed peptide which, in association with MHC-encoded molecules, contributes to *graft rejection*, albeit not usually as severe as that due to MHC mismatch.
[3]

mitogen (n)**, /ic** (adj)
Substance that induces *lymphocyte* transformation or, more generally, mitosis and cell proliferation.
[5]
Note: Mitogens most commonly employed in *immunotoxicology* assays include the *T cell* mitogens *concanavalin A (ConA)* and *phytohemagglutinin (PHA)*. Mitogens routinely used for assessing *B cell* proliferation include *pokeweed mitogen (PWM)*, which can also act on T cells, and Escherichia coil *lipopolysaccharide (LPS)*.

mitogen-activated protein kinase (MAPK)
Member of a kinase network in which 'upstream' kinases activate 'downstream' kinases that, in response to phosphorylation, translocate to the nucleus and activate transcription factors.
Note: These include the extracellular regulated kinases (Erk), stress-activated protein kinase (SAPK or p38), and the kinase of the c-jun oncoprotein (JNK).

mitophagy
Autophagy-related pathway specific for mitochondria; it can be subdivided into macromitophagy and micromitophagy depending upon the degree of mitophagy.

mixed lymphocyte response/reaction (MLR)
T cell-proliferative response induced by cells expressing *allogeneic major histocompatibility complex (MHC) molecule*s.
[3]

mixed connective tissue disease (MCTD)
Sharp's syndrome
Human *autoimmune disease* in which the *immune system* attacks the body, producing symptoms that combine features of polymyositis, *systemic lupus erythematosus (SLE)*, and *systemic scleroderma*, and thus being considered as an overlap syndrome.
Note 1: MCTD commonly causes joint pain/swelling, *Raynaud phenomenon*, muscle *inflammation*, and scarring of the skin of the hand. It does not

typically cause kidney disease or seizures.

Note 2: Distinguishing laboratory characteristics are a positive, speckled *anti-nuclear antibody (ANA)* and an anti-U1-RNP antibody.

molecular mimicry (in immunology)
Concept that identity or similarity of *epitope*s expressed by a pathogen and by a self molecule may lead to production of *antibodies* reacting to the *self-antigen*.

Note: This may explain how some *autoimmune disease*s develop.

monoclonal antibody
Antibody derived from a single *B cell clone* and therefore bearing identical *antigen*-binding sites and *isotype* to other members of the clone.
After [3]

monocyte
Mononuclear *phagocyte* found in blood and which is the precursor of the tissue *macrophage*.
[3]

Note 1: Formed in the *bone marrow* from the promonocyte, monocytes are transported to tissues, as of the lung and liver, where they develop into macrophages.

Note 2: Formerly called large mononuclear *leukocyte* and hyaline or transitional leukocyte.

monokine
Alternative name for a *cytokine* produced by *monocyte*s.

mononuclear phagocyte system (MPS)
reticuloendothelial system (RES)
Network of phagocytic cells (see *phagocyte*) throughout the body. System comprising blood *monocyte*s and tissue *macrophage*s.
After [3]

mouse IgE test (MIGET)
Procedure in which serum *immunoglobulin E (IgE)* levels are measured in mice following topical exposure to a test substance. Substances that cause a significant increase in IgE are considered to be potential respiratory *allergen*s.

mouse ear-swelling test (MEST)
Test for sensitization in which the test substance is applied topically to the ear of a mouse for three consecutive days. The change in ear thickness is then measured following *challenge* on day 8.

mucocutaneous
Pertaining to or affecting the mucous membranes and (or) the skin.

mucosa
Moist tissue that lines some organs and body cavities, including the nose, mouth, lungs, and digestive tract.

mucosa-associated lymphoid tissue (MALT)
Secondary lymphoid tissue present in the surface *mucosa* of the respiratory tract and bronchus (*BALT*), gastrointestinal tract (*GALT*), nasal passages (*NALT*), larynx (LALT), conjunctiva (CALT), and genitourinary tract, and in the skin sub-epidermis (SALT).

Note: MALT plays an important part in limiting entry of pathogens through the mucosal surfaces.

mucosal addressin cell adhesion molecule-1 (MAdCAM-1)
Protein involved in trafficking of *lymphocyte*s to *mucosa*l endothelium.

Note: Expression of MAdCAM-1 is induced in the murine endothelial cell line bEnd.3 by *tumor necrosis factor α (TNF-α)*, *interleukin (IL)*-1, and bacterial *lipopolysaccharide (LPS)*.

mucosal tolerance
State of *lymphocyte* hyporesponsiveness to protein *antigen*s applied across *mucosa*l surfaces by oral or nasal instillation.

multiple chemical sensitivity (MCS)
idiopathic environmental intolerance
Intolerance condition attributed to extreme sensitivity to various environmental chemicals, found in air, food, water, building materials, or fabrics.

Note 1: This syndrome is characterized by the patient's belief that his or her symptoms are caused by very low-level exposure to environmental chemicals. The term "chemical" is used to refer broadly to many natural and man-made substances, some of which have several chemical constituents.

Note 2: Several theories have been advanced to explain the cause of multiple chemical sensitivity, including *allergy*, toxic effects, and neurobiological sensitization. There is insufficient scientific evidence to confirm a relationship between any of these possible causes and symptoms.

[5]

multiple myeloma
Plasma cell malignancy resulting in high levels of monoclonal *immunoglobulin (Ig)* in *serum* and of free *light chain*s (*Bence–Jones protein*) in urine.
[3]
See also *myeloma*.

multiple sclerosis
Disease of the central nervous system, believed to be *autoimmune*, in which an *inflammatory response* results in demyelination of neurons and loss of neurological function.

multiplex immunoassay
Type of particle *immunoassay* employing sets of microspheres with various physicochemical features, each labeled with a different *antibody*. The method allows detection in a single measurement of an array of 100 or more proteins.
See also *particle immunoassay*.

multipotent progenitor cell
Undifferentiated *stem cell*, obtained from adult *bone marrow* or other non-embryonic tissue sources, that possesses the ability to differentiate into a variety of cell types, especially into cells of a closely related family of cells that are expanded in vitro and deposited in master cell banks for 'off-the-shelf' use, with potential *hematopoiesis*-inducing and immunomodulating activities.

Note 1: Allogeneic multipotent adult progenitor cells (MAPCs) are non-immunogenic due to the lack of *major histocompatibility complex (MHC) molecule* expression, and so elicit no *immune response* upon administration.

Note 2: In vivo, bone marrow-derived adult stem cells are capable of maturing into a broad range of cell types and may help to restore the *immune system* by producing multiple therapeutic molecules in response to *inflammation* and tissue damage.

murine local lymph node assay (LLNA)
Predictive test of sensitization in which a test substance is applied topically to the skin of mice (usually three times at daily intervals) and the weight of the local *draining lymph node*s is measured at six days. Usually *lymphoproliferation* in the nodes is measured following injection of [^{3}H]thymidine or bromodeoxyuridine.

mutation (in immunology)
See *somatic hypermutation*.

myasthenia gravis, acquired
Autoimmune disease characterised by muscle weakness usually affecting ocular and oropharyngeal muscles due to an *autoimmune* attack against components of the neuromuscular junction (e.g., the nicotinic acetylcholine receptor).

Note: This disease may be *idiopathic*, paraneoplastic [*thymic* tumor or lung (*Lambert-Eaton myasthenic syndrome*) tumor, etc.], or drug-induced (e.g., D-penicillamine).

After [1]

myelodysplastic syndrome
preleukemia (obsolete)
Diverse collection of hematological conditions united by ineffective production (or dysplasia) of *myeloid* blood cells and risk of transformation to *acute myelogenous leukemia (AML)*. *Anemia* requiring chronic blood *transfusion* is frequently present.

myeloma

Tumor composed of cells derived from hematopoietic cells (see *hematopoiesis*) of the *bone marrow*, or from *mast cell*s.
See also *Bence-Jones protein*, *multiple myeloma*.

myeloid
myelogenous
Referring to the nonlymphocytic groups of white blood cells, including *granulocyte*s, *monocyte*s, and *platelet*s.

Note: Acute myelogenous leukemia (AML) is also known as acute myeloid leukemia.

myeloid stem cell
One of two groups of *stem cell*s produced in the *bone marrow*. Myeloid stem cells may mature into several types of blood cells, including acidic *basophil*s, *eosinophil*s, *erythrocyte*s, *macrophage*s, *megakaryocyte*s, and *neutrophil*s.

myeloid tissue
Tissue within red *bone marrow* that produces the blood cells. It is found around the blood vessels and contains various cell types that are precursors of the blood cells.

myeloma protein
Monoclonal antibody secreted by *myeloma* cells.
[3]

myeloperoxidase (MPO)
Enzyme found in azurophilic granules of *neutrophil*s, the major target of *antineutrophil cytoplasmic autoantibody (ANCA)*.

Note 1: MPO *autoantibodies* are diagnostic markers for microscopic polyangiitis, rapidly progressive *glomerulonephritis*, and *Goodpasture disease* or *syndrome*.

Note 2: MPO autoantibodies are also found in patients exposed to silica or drugs (e.g., hydralazine, propylthiouracil, D-penicillamine) as well as in some patients with *Wegener granulomatosis (WG)* and other *autoimmune disease*s.

After [1]

myelopoiesis
Process of formation and development of *myeloid* blood cells in the *bone marrow*.

myelosuppression
Decrease in *myeloid* cells, including *pancytopenia*, *anemia*, *leukopenia*, *lymphopenia*, *thromocytopenia*, and other *blood dyscrasia*s.

myositis, autoimmune
Rare *systemic* inflammatory myopathy, including primary polymyositis, primary dermatomyositis, myositis associated with malignancy, childhood dermatomyositis, and

myositis with multisystem *autoimmune disease* [e.g., *mixed connective tissue disease (MCTD)*, *systemic sclerosis (SSc)*].

Note: Autoantibodies against aminoacyl-tRNA synthetases (e.g., anti-Jo-1), signal recognition particles (e.g., anti-SRP54), nuclear helicase (anti-Mi-2), tRNA and tRNA–protein complexes (e.g., anti-Mas), and translation factor (anti-KJ) have been described as myositis-specific.

NACHT domain-, leucine-rich repeat (LRR)-, and pyrin (N-terminal homology) domain (PYD)-containing protein 3 (NALP3, NLRP3)
cryopyrin
NOD-like receptor (NLR), found in certain *inflammasome*s, that binds to aggregated proteins and the peptides that compose them. Its activation leads to the generation of inflammatory *cytokine*s, such as *interleukin (IL)*-1, and neurotoxic factors.

Note: Mutations in NALP3 are responsible for the autoinflammatory diseases familial cold autoinflammatory syndrome, Muckle-Wells syndrome and neonatal onset multisystem inflammatory disease.

NADPH oxidase
See *respiratory burst.*

NK cell
See *natural killer (NK) cell*.

NKT cell
See *natural killer T (NKT) cell*.

N-nucleotides
Non-templated nucleotides added to the junctions between *antibody* and *T-cell receptor (TCR) variable (V) gene*, *diversity (D) gene*, and *joining (J) gene* segments during gene rearrangement.
[3]

NOD-like receptor (NLR)
Any of a large family of cytoplasmic proteins containing a nucleotide-binding domain and *leucine-rich repeat*s *(LRR),* involved in regulation of *inflammation* and *apoptosis*; many family members are thought to function as *pattern recognition receptor*s *(PPR)*.

N-region
Highly *variable region* on the *H-chain* of *immunoglobulin*s.

naïve lymphocyte
Mature *T cell* or *B cell* that has not yet been activated (see *lymphocyte activation*) by encounter with *antigen*.
[3]

nasal-associated lymphoid tissue (NALT)

See *mucosa-associated lymphoid tissue (MALT)*.

natural autoantibodies (NAA)
Part of the naturally occurring repertoire of polyreactive *antibodies* that bind to *autoantigen*s with low *affinity*. They are mainly of *immunoglobulin M (IgM) isotype* and produced by *CD5+ B lymphocyte*s.

Note 1: Natural antibodies and their producing cells may have a physiological role in the following processes: (i) first line of protection against external invaders, (ii) elimination of degraded autoantigens and senescent cells, and (iii) tolerization (see *tolerance*) of *T cell*s by presenting autoantigens, thereby in protecting from development of pathological *autoimmunity*.

Note 2: In contrast, natural autoantibodies may become pathogenic in clonal B cell disorders, e.g., *monoclonal* anti-I *antibodies* in cold agglutinin disease cause *autoimmune hemolytic anemia*.

After [1]

natural immunity
Host defense mechanisms that do not require prior exposure to *antigen*.

Note: Nonimmunological defense may involve the actions of *macrophage*s and *natural killer (NK) cell*s, mucocutaneous or integumental barriers, the action of cilia or microvilli, or physiological processes, e.g., urinary outflow, vascular perfusion of tissues, or the presence of native flora, which 'outcompete' pathogens.

natural killer (NK) cell
Large granular *lymphocyte* which does not rearrange nor express either *immunoglobulin* or *T-cell receptor (TCR)* genes but is able to recognize and destroy certain tumor and virally infected cells in a *major histocompatibility complex (MHC) molecule*- and *antibody*-independent manner.
[3]

natural killer cell activity assay
Immunotoxicity test in which *lymphoid tissue* or blood that has been treated with a test compound is co-incubated with target cells. The cytotoxic effect on target cells is measured, e.g., with the *chromium release assay*. It is used under circumstances where differences from untreated cells are attributed to *natural killer (NK) cell* activity.

natural killer T (NKT) cell
Lymphoid cells with a morphology and granule content intermediate between *T cell*s and *natural killer (NK) cell*s.

Note: NKT cells express low levels of α:β *T cell receptor* with an invariant α chain and very restricted β chain specificity, recognize lipid and glycolipid *antigen*s presented by the nonclassical *MHC*- like molecule CD1d, and are potent producers of *interleukin (IL)*-4 and *IFN*-γ.

After [3]

natural regulatory T cell
See *regulatory T cell (Treg)*.

natural resistance-associated macrophage protein (NRAMP)-1
Iron transporter that plays a critical role in *macrophage activation* and differentiation.

Note: Allele 3 of the NRAMP-1 promoter is associated with *autoimmune* disorders [e.g., *rheumatoid arthritis (RA)*, juvenile rheumatoid arthritis, *diabetes mellitus type 1*, *multiple sclerosis*].

After [1]

necro/sis (n), /**tic (**adj)
Sum of morphological changes resulting from cell death by lysis and (or) enzymatic degradation, usually accompanied by *inflammation* and affecting groups of cells in a tissue.

Note: Distinct from *apoptosis*, *autophagy*, and other modes of programmed cell death.

After [5]

negative selection
Deletion by *apoptosis* in the *thymus* of *T cell*s that recognize self-peptides presented by self-*major histocompatibility complex (MHC) molecule*s, thus preventing the development of *autoimmune* T cells. Negative selection of developing *B cell*s is also thought to occur if they encounter high levels of *self-antigen* in the *bone marrow*.
[3]

neoantigen
Antigen newly expressed on a tumor or virally infected cell, or arising after macromolecule-*hapten* binding.

neonat/e (n), /**al** (adj)
Infant during the first 4 weeks of postnatal life.

Note: For statistical purposes, some scientists have defined the period as the first 7 days of postnatal life. The precise definition varies from species to species.

After [5]

neonatal tolerance
Tolerance to specific foreign *antigen*s induced by the exposure of a bird or mammal to the foreign antigens during embryonic or *neonatal* life, depending upon species.

nephritis, autoimmune
Inflammation of the kidney due to immunological reaction to renal *antigen*s.

Note: Common examples are anti-glomerular basement membrane disease (*Goodpasture disease* or *syndrome*), *autoimmune* tubulointerstitial *nephritis* with antibody to tubular basement membrane, or occurring as part of *systemic autoimmune disease*s independent of renal *autoantigen*s [*lupus*

nephritis in *systemic lupus erythematosus (SLE)*, interstitial nephritis in *Sjögren syndrome*, nephritis in *ANCA-associated vasculitis*, *cryoglobulinemic vasculitis*, or hypo*complement*emic urticarial vasculitis syndrome].

After [1]

nettle rash
See *hives*.

neuropathy, autoimmune
Autoimmune disease of the nervous system.

Note 1: More and more neuropathies are described as autoimmune or possibly autoimmune in nature. Little is known about *xenobiotic*s in the pathogenesis, but infections may play an important role in the initiation of some diseases.

Note 2: Autoimmune neuropathies may be manifested at the neuromuscular junction, as central nervous system diseases (e.g., *multiple sclerosis*, *paraneoplastic autoimmune syndrome*s, stiff-person syndrome, as well as manifestations of *systemic* autoimmune diseases), and diseases of the peripheral nerves (e.g., various forms of acute and chronic demyelinating neuropathies).

After [1]

neutralization (in immunology)
Blocking by an *antibody* of the effects of a virus.

neutropenia
Abnormally low concentration of *neutrophil*s in the blood.

Note: Neutropenia is associated with an increased risk of infection.

neutrophil
polymorphonuclear leucocyte
Granular *leukocyte*, the major circulating phagocytic polymorphonuclear *granulocyte*, having a nucleus with three to five lobes and fine cytoplasmic granules stainable by neutral dyes.

Note 1: The cells have properties of *chemotaxis*, adherence to *immune complex*es, and *phagocytosis*.

Note 2: The cells are involved in a variety of inflammatory processes including late-phase *allergic* reactions and are also able to mediate *antibody-dependent cellular cytotoxicity (ADCC)*.

Modified from [1]
See also *phagocyte*.

neutrophil activation
Change in morphology and behavior of a *neutrophil* resulting from exposure to a *cytokine*, *chemokine*, cellular *ligand*, or soluble factor.

See also *lymphocyte activation*.

nitric oxide
Generic term for nitrogen monoxide species, including nitrosonium ion, nitric oxide radical, etc., that can function in a cell-signaling capacity.

nondepleting antibody
Cell surface *antibody* that does not provoke attack by *killer cell*s and thus does not provoke depletion of a group of cells in the body, usually referring to *B cell*s.

non-Hodgkin lymphoma
Any of various malignant *lymphoma*s characterized by the absence of *Reed-Sternberg cell*s and producing symptoms similar to those of *Hodgkin disease*.

non-obese diabetic (NOD) **mouse**
Genetically modified mouse with a susceptibility to spontaneous development of *automimmune diabetes mellitus type I*.

non-self
Of, relating to, or designating a cell or tissue that has not been produced by the individual organism.

Note: Non-self molecules are identified by the *immune system* as foreign or abnormal, thus provoking an *immune response*.

nuclear factor of activated T cells (NFAT)
Transcription factor involved in rapid cell response to stress, such as injury or invading pathogens, and in cell proliferation and survival.

nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB)
Protein complex that controls the transcription of genes involved in *cytokine* production, *cellular adhesion*, *inflammation*, and *apoptosis*.

Note: NFκB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet irradiation, oxidized low-density lipoprotein (LDL), and bacterial or viral *antigen*s.

nucleotide-binding oligomerization domain-containing protein 1, 2 (NOD1, NOD2)
Any member of a family of human intracellular proteins involved in the detection of invasive bacteria and activation of the *NFκB* transcription factor pathway.

Note: In epithelial cells, NOD1 is essential for sensing intracellular Gram-negative bacteria through a tripeptide motif in the bacterial peptidoglycan.

After [26]

nucleotide-binding oligomerization domain-containing protein (NOD)**-like receptor** (NLR)
NOD-like receptor protein (NLRP)

Cytosolic protein that contains a central nucleotide-binding oligomerization domain, an N-terminal effector-binding domain and C-terminal leucine-rich repeats (LRR).

Note 1: NOD-like *receptor*s have been implicated as mediators of protective *immune response*s against intracellular pathogens.

Note 2: Genetic associations of polymorphisms in NOD-like receptor genes with complex chronic inflammatory barrier diseases, such as *Crohn disease* and *asthma*, and with rare auto-inflammatory syndromes including familial cold urticaria, Muckle-Wells syndrome and *Blau syndrome* have been described.

See also *NACHT domain-, leucine-rich repeat-, and PYD-containing protein 3 (NALP3, NLRP3)*.

[27]

nude mouse

Mouse which is *T cell*-deficient due to a homozygous gene defect (*nu*/*nu*) resulting in the absence of a *thymus* (and also lack of body hair).

[3]

null cell

Lymphocyte with neither *T*- nor *B-cell differentiation antigen*s on its surface.

OKT3

Brand name for muromonab-CD3, an *immunosuppressant* drug given intravenously to reverse acute *rejection* of transplanted organs, including the heart, kidneys and liver.

Note: OKT3 was the first *monoclonal antibody* used to treat patients.

See also *antibody therapy*.

oligoclonal

Having a few different *clone*s, or the product of a few different clones.

After [3]

oncofetal antigen

Antigen whose expression is normally restricted to the fetus but which may be expressed during malignancy in adults.

[3]

opsonin

Substance, e.g., *antibody* or C3b, which enhances *phagocytosis* by promoting adhesion of the *antigen* to the *phagocyte*.

[3]

opsonization

Coating of *antigen* with an *opsonin* to enhance *phagocytosis*.

Note: The interaction of opsonized complexes with *Fc receptor*s or *complement receptor*s facilitates their uptake by the receptor-bearing *phagocytic cell*s.

After [1]

oral tolerance
Orally induced and immune-mediated non-responsiveness.
[1]
See also *tolerance*.

oral vaccination
Immunization against a pathogen with a *vaccine* administered by mouth.

Ouchterlony technique
Ouchterlony double diffusion assay
Double-radial immunodiffusion procedure for the detection of *precipitating antibodies*.
Note: Method of high diagnostic specificity but low sensitivity.
After [1]

oxidative burst
See *respiratory burst*.

P-nucleotides
Palindromic nucleotide sequences generated at the junctions between *antibody* and *T-cell receptor (TCR) variable (V)*, *diversity (D)* and *joining (J) gene* segments during gene rearrangement.
[3]

P-selectin
Cell *adhesion molecule* expressed on the surface of activated endothelial cells and *platelet*s.

pancytopenia
Decrease in the number of red blood cells, white blood cells, and *platelets*.

paracortical area
paracortex
Region of a *lymph node* enriched in *T lymphocyte*s.

paracrine
Type of signaling in which a cell secretes a chemical messenger that binds to *receptor*s on nearby cells, leading to changes in those cells. Thus, describing or relating to a regulatory cell that secretes an agonist into intercellular spaces in which it diffuses to a target cell other than that which produces it, or describing or relating to such an agonist.
After [26]
See also *autocrine*.

paramone
Paracrine agonist.

paraneoplastic autoimmune syndrome

Any of several *autoimmune disease*s that are caused by tumor-induced perturbations of the *immune system* with damaging effects on various organ systems (e.g. cancer-associated retinopathy, paraneoplastic neurological syndromes, paraneoplastic cutaneous syndromes). In most cases, *autoantibodies* generated by antitumor *immunity* are responsible for the tissue injury.
[1]
See also *Lambert-Eaton myasthenic syndrome (LEMS)*.

paratope
Site in the variable region of an *antibody* or *T-cell receptor (TCR)* that binds to an *epitope* of an *antigen*.

particle immunoassay
Immunoassay in which *antibody* is bound to the surface of microspheres. After incubation with the *antigen*-containing biological fluid, and subsequent manipulation, detection is usually performed by *flow cytometry*.

passive cutaneous anaphylaxis (PCA) **test**
Assay for *allergen*icity in which an *antibody* is injected intradermally into a test animal followed at a later time (anywhere from 3-48 h) with an intravenous injection of a mixture of a test *antigen* and a dye (typically Evans blue). Increased vascular permeability at the site of antigen-antibody reaction is visualized by extravasation of the dye.

passive hemagglutination
Method of measuring *antibody titer*, in which *antigen*-coated *erythrocyte*s are agglutinated (see *agglutination*) by adding antibody specific for the antigen.

passive immunization
Immunization of an individual by the transfer of *antibody* synthesized in another individual.

patch test
Test for *allergy* that is performed by placing the suspected *allergen* in direct contact with the skin or *mucosa*.

pathogen-associated molecular pattern (PAMP)
Describing repetitive motifs of molecules such as lipopolysaccharide, peptidoglycan, lipoteichoic acids and mannans, which are widely expressed by microbial pathogens but are not present on *host* tissues. They are therefore utilized by the *pattern recognition receptor*s *(PRR*s*)* of the *immune system* to distinguish pathogens from *self-antigen*s.
[3]

pattern recognition receptor (PRR)
Receptor found on many different cell types in the *immune system* that enables them to recognize *pathogen-associated molecular pattern*s *(PAMP*s*)*. Amongst the large

number of different PRRs are the mannose receptor (CD206), *macrophage* scavenger receptor (CD204) and the *Toll-like receptor*s.
[3]

Note: Many of the *NOD-like receptor*s *(NLR*s*)* are thought to serve as PRRs.

pauci-immune
Referring to *vasculitis* characterized by relatively little deposition of *immunoglobulin (Ig)* and *complement* factors, usually describing a form of *glomerulonephritis*.

pemphigus
pemphigus vulgaris
Rare, serious *autoimmune disease* marked by successive outbreaks of blisters, which appear suddenly and disappear leaving pigmented spots.

Note: Other mucous membranes, as well as the skin, are usually affected and the disease may be fatal.

peptide tetramer
Structure consisting of four identical *major histocompatability complex* (*MHC)*-encoded peptides, presenting four binding sites for biotin attached to the tail of the MHC molecule, and held together by fluorescent streptavidin.

peptide vaccine
Preparation of an immunologically active peptide found in a disease-causing organism or substance, or any of their products, which is specially treated for use in *vaccination*.

peptide-binding groove
Structural feature found in *major histocompatibility complex (MHC) class I* and *class II* heterodimeric proteins that can bind endogenous peptides.
See also *antigen-presenting groove*.

perforin
Molecule produced by *cytotoxic T cell*s and *natural killer (NK) cell*s that, like *complement* component C9, polymerizes to form a pore in the membrane of the *target cell* leading to cell death.
[3]

periarteriolar lymphoid sheath (PALS)
Lymphoid tissue that forms the *white pulp* of the *spleen*.
[3]

periodontitis
Inflammatory reaction of the tissues surrounding a tooth (periodontium), usually resulting from the extension of gingival *inflammation* (gingivitis) into the periodontium, and involving inflammation and infection of the ligaments and bones that support the teeth.

peripheral blood leukocyte (PBL)
Leukocyte derived from the peripheral circulatory system.

peripheral blood mononuclear cell (PBMC)
Monocyte produced by the *bone marrow* from *hematopoietic stem cell* precursors, circulating in the bloodstream for about one to three days before moving into tissues throughout the body.

Note: PBMCs constitute between three to eight percent of the *leukocyte*s in the blood. In the tissues monocytes mature into different types of *macrophage*s at different anatomical locations [see *macrophage, resident(ial)*].

peripheral lymphoid organ
Any of the lymphoid organs (see *lymphoid tissue*) other than the *thymus*.

peripheral neuropathy, autoimmune
Acute or chronic inflammatory neuropathy leading to demyelination and axonal damage of nerves and nerve roots associated with high-*titer*ed *autoantibodies* against gangliosides [e.g., *Guillain-Barré syndrome (GBS)*, Miller-Fisher syndrome, acute sensory ataxic neuropathy].
[1]

peripheral tolerance
Specific immunological *tolerance* occurring outside of the primary lymphoid organs (see *lymphoid tissue*).
[3]

pernicious anemia
Disease in which the *erythrocyte*s are abnormally formed, due to an inability to absorb vitamin B_{12}. True pernicious anemia refers specifically to a disorder of atrophied parietal cells leading to absent intrinsic factor, resulting in an inability to absorb B_{12}.

Note 1: This is the end stage of 10–15% of *autoimmune* gastritis.

Note 2: This disease is associated with a variety of autoimmune endocrine diseases (e.g., *Hashimoto thyroiditis*, *Addison disease* and autoimmune myasthenic syndromes).

Modified from [1]

pexophagy
Autophagy selective for degradation of peroxisomes, which can be separated into macropexophagy and micropexophagy.

Peyer's patch
Part of the *gut-associated lymphoid tissue (GALT)* and found as a distinct lymphoid nodule, mainly in the small intestine.
After [3]

phage antibody library

Collection of *cloned antibody variable (V) region* gene sequences that can be expressed as *Fab* or scFv fusion proteins with bacteriophage coat proteins. These can be displayed on the surface of the phages. The gene encoding a recombinant *monoclonal antibody* is enclosed in the phage particle and can be selected from the library by binding of the phage to specific *antigen*.
[3]

phage display library
See *phage antibody library*.

phagocyte
Cell, especially of *monocyte*/*macrophage* or *neutrophil* lineage, that is specialized for the engulfment of cellular and particulate matter.
After [3]

phagocytic activity assay
phagocytosis assay
Method of quantifying *phagocytosis* in which yeast cells, stained with May-Grünwald stain, are incubated with *macrophage*s, and subsequently, after a fixed time, yeast cells engulfed in the macrophages are counted.

phagocytosis
Process by which particulate material is endocytosed by a cell.
See also *endocytosis*, *pinocytosis.*
[5]

phagocytosis assay
See *phagocytic activity assay*.

phagolysosome
Intracellular vacuole where killing and digestion of phagocytosed material occurs following the fusion of a *phagosome* with a *lysosome*.
[3]
See also *phagocytosis*.

phagosome
Intracellular vacuole produced following invagination of the cell membrane around phagocytosed material.
[3]
See also *phagocytosis*.

Philadelphia chromosome
Chromosome resulting from a reciprocal translocation between human chromosomes 9 and 22, most commonly associated with *chronic myelogenous leukemia (CML)*.
See also *ABL oncogene*.

phorbol myristate acetate (PMA)
tetradecanoyl phorbol acetate (TPA)
Mitogenic phorbol ester that directly stimulates *protein kinase C (PKC)* and acts as a tumor promoter.
[3]

phospholipase Cγ (PLC-γ)
Enzyme that cleaves phosphatidylinositol bisphosphate into diacylglycerol and inositol trisphosphate, leading to the activation of two major cell signaling pathways.
Note: One consequence of the signaling is *B-* and *T lymphocyte activation*.

photoallergy
Type IV hypersensitivity reaction in which photoactivation of a substance produces a *hapten* that then acts as a *sensitizer*.

photocontact dermatitis
Type of *contact dermatitis* arising when substances are transformed into either irritants or *allergen*s upon exposure to light.
Note: Aftershave lotions, sunscreens, and certain topical sulfa drugs may be changed into allergens, while coal tar and certain oils used in manufacturing may become irritants after exposure to sunlight.

photosensitivity
Skin reddening due to an abnormal reaction to sunlight, characteristic of *systemic autoimmune disease*s [e.g., *systemic lupus erythematosus (SLE)*, *mixed connective tissue disease (MCTD)*], and cutaneous and subacute cutaneous lupus erythematosus.
[1]

phototoxicity test
Procedure used to identify the phototoxic potential of a test substance. The substance is administered either *systemic*ally or topically on the skin, and light is subsequently shone on the skin to photoexcite the substance.
Note: There is also an in vitro test using photoexposure of treated Balb c/3T3 cells followed by viability testing.

phytohemagglutinin (PHA)
Plant *lectin* that acts as a *T cell mitogen*.
[3]

pinocytosis
Type of *endocytosis* in which soluble material is taken up by the cell in a liquid phase and incorporated into vesicles.
After [5]

placental barrier
See *blood-placental barrier*.

plantibody
Animal *antibody* (or fragment thereof), expressed in a genetically-modified plant.

plaque assay
See *anti-sheep red blood cell (SRBC) IgM response assay*.

plaque forming cell (PFC)
Antibody-secreting *plasma cell* detected *in vitro* by its ability to produce a 'plaque' of lysed *antigen*-sensitized *erythrocyte*s in the presence of *complement*.
[3]
See also *plaque assay*.

plasma
1. Fluid component of blood in which the blood cells and *platelet*s are suspended.
2. Fluid component of semen produced by the accessory glands, the seminal vesicles, the prostate, and the bulbo-urethral glands.
3. Cell substance outside the nucleus (i.e., the cytoplasm).
[5]

plasmablast
Highly proliferative cell that is a developmental intermediate between small *B lymphocyte*s and *immunoglobulin (Ig)*-secreting mature *plasma cell*s.

plasma cell
Terminally differentiated *B lymphocyte*, with little or no capacity for mitotic division, that actively secretes large amounts of *antibody*.

Note: Plasma cells have eccentric nuclei, abundant cytoplasm, and distinct perinuclear haloes. The cytoplasm contains dense rough endoplasmic reticulum and a large Golgi complex.

Modified from [1]

plasmacytoid dendritic cell
Dendritic cell of distinct lineage, found in blood and peripheral *lymphoid tissue,* which secretes large amounts of *interferon (IFN)* upon activation.
After [2]

plasmacytoma
Mass of neoplastic monoclonal *plasma cell*s growing in bone or soft tissue.

plasma exchange
See *plasmapheresis*.

plasmapheresis
plasma exchange
Technique of extracorporeal separation of blood cells from *plasma*, with return of the

cells to the patient.
Note: Frequently used to remove *antibodies* in *autoimmune disease*.

platelet
thrombocyte
Small irregular or disc-shaped cell found in large numbers in mammalian blood, essential for blood clotting.

platelet activating factor (PAF)
Alkyl phospholipid released by a variety of cell types including *mast cell*s and *basophil*s, which has immunoregulatory effects on *lymphocyte*s and *monocyte*s/*macrophage*s, as well as causing *platelet* aggregation and *degranulation*.
After [3]

platelet-derived growth factor (PDGF)
Protein synthesized by *platelet*s that is released into the *serum* during blood clotting.
Note: PDGF represents the major growth factor in human serum and is a potent *mitogen* for connective tissue and glial cells.

pluripotent stem cell
Self-replicating cell capable of developing into cells and tissues of the three primary embryonic germ layers.

pokeweed mitogen (PWM)
Plant *lectin* which is a *T cell*-dependent *B cell mitogen*.
[3]

pollenosis
See *hay fever*.

polyarteritis nodosa
disseminated necrotizing periarteritis
panarteritis
periarteritis
periarteritis nodosa
Systemic disease characterized by widespread *inflammation* of small and medium-sized arteries in which many of the foci are nodular.

polyclonal
Many different *clone*s, or the product of many different clones, e.g., polyclonal *antiserum*.
[3]

polyclonal activator
Substance that induces *activation* of multiple clones of *B lymphocyte*s or *T lymphocyte*s.
After [7]

See also *mitogen*.

polyendocrinopathy, autoimmune
Autoimmune disease affecting multiple endocrine organs.

Note 1: (i) The autoimmune polyglandular syndrome type 1 is characterized by mucocutaneous candidiasis in association with endocrine manifestation (also called APECED syndrome, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy).
(ii) The autoimmune polyglandular syndrome type 2 exhibits any combination of adrenal insufficiency (see *Addison disease*), *diabetes mellitus type 1*, lymphocytic thyroiditis (see *thyroiditis*, *autoimmune*), *hypoparathyroidism*, and gonadal failure.

Note 2: In both types, organ-specific *autoantibodies* against a variety of endocrine glands are detectable.

After [1]

poly I:C
Polyinosinic:polycytidylic acid, a synthetic immunostimulant mimicking viral double stranded RNA.

poly ICLC
Polyinosinic:polycytidylic acid, poly-L-lysine, and carboxymethylcellulose (letter roots of the acronym underlined), a synthetic immunostimulant mimicking viral double stranded RNA.

poly-Ig receptor
Receptor molecule that specifically binds *J chain*-containing polymeric *immunoglobulin (Ig)*, i.e., dimeric secretory *immunoglobulin A (IgA)* and pentameric *immunoglobulin M (IgM)*, and transports it across *mucosa*l epithelium.
[3]

polymorphism (general)
Variability in shape or structure

polymorphism (in genetics)
Occurring in more than one form within a species owing to the existence of multiple *allele*s at a particular genetic locus.

polymorphism (in metabolism)
polymorphia (in metabolism)
Interindividual variations in metabolism of endogenous and exogenous compounds due to genetic influences, leading to enhanced side effects, or to toxicity of drugs, or to different clinical effects (as in variation in metabolism of steroid hormones).
After [5]

polymorphonuclear granulocyte

See *polymorphonuclear leukocye*.

polymorphonuclear leukocyte
Mature *leukocyte* with granular cytoplasm and a segmented and irregularly shaped nucleus.

Note 1: It is the predominating leukocyte in the blood and is found in the tissues during acute inflammatory processes and in the superficial surface aspects of a lesion during subacute or chronic *inflammation*.

Note 2: There are three major types: *neutrophil*s, *eosinophil*s, and *basophil*s.

polymyositis
Disorder characterized by *inflammation* and degeneration of skeletal muscle, causing pain, weakness, and wasting in affected (usually proximal) muscles.

popliteal lymph node assay (PLNA)
Test for immunosensitization measuring popliteal *lymph node* hyperplasia after subcutaneous injection of a test substance into the footpad of the hindpaw of a rodent.

positive selection
Selection of those developing *T cell*s in the *thymus* that are able to recognize self-*major histocompatibility complex (MHC) molecule*s. This occurs by preventing *apoptosis* in these cells.
[3]

pre-B cell
Cell in the *B lymphocyte* lineage that has rearranged *heavy chain* but not *light chain* genes; it expresses surrogate light chains and m heavy chain at its surface in conjunction with *immunoglobulin*s Ig a and Ig b. All these molecules comprise the pre-B cell *receptor* (pre-BCR).
After [7]

precipitating antibody
Antibody that is capable of reacting with a soluble *antigen* with the formation of an insoluble antigen/antibody complex.
[26]
See also *precipitin*.

precipitin
Precipitate of *antibody* and multivalent *antigen* due to the formation of high molecular weight complexes.
[3]

pre-T cell
thymocyte
Cell differentiating into a *T lymphocyte* in the *thymus* gland.

Note: During maturation thymocytes express on their surface a precursor *T-cell*

receptor (TCR) called a pre-T-cell receptor, and both *CD8* and *CD4* proteins (*double-positive cell*s). At the same time they slowly migrate from the outer cortex of the thymus to the inner medullary region. Only the 2% of cells capable of distinguishing *self-antigen* survive to maturity in the *medulla*. Here they become *single-positive cell*s, expressing exclusively CD4 or CD8 surface proteins, and are exported from the thymus in the bloodstream to become *helper T cell*s *(Th)* and *cytotoxic T cell*s, respectively.

After [28]

prick test

Test carried out by placing a drop of a suspected *allergen*ic extract on the skin of the forearm and gently pricking it into the upper layer of skin. Sensitivity to a substance is indicated if the spot swells slightly and becomes red within about fifteen minutes.

Note: A positive result is far from conclusive and, at best, gives a vague indication of allergenicity. The prick test is inappropriate as a test for food allergens.

primary biliary cirrhosis (PBC)

Autoimmune liver disease that results in the destruction of bile ducts, leading to fibrosis and cirrhosis.

Note: Primary biliary cirrhosis-specific *antibodies* are *antimitochondrial antibodies (AMA)* directed against proteins of the pyruvate dehydrogenase complex (mainly the E2 subunit).

After [1]

primary challenge

See *primary response*.

primary immune response

Immune response to the first encounter with an *antigen*, characterized by slow production of *antibody* molecules and the *priming* of *lymphoid tissue* in readiness for the production of a *secondary immune response* on subsequent *challenge* with the same antigen.

Note: The primary response is generally weak, has a long induction phase or lag period, consists primarily of the release of *immunoglobulin M (IgM)* antibodies, and generates immunologic *memory*.

primary immunization

First introduction of a *vaccine* into the body for the purposes of inducing *immunity*.
See also *primary immune response*.

primary lymphoid follicle

Region of a *secondary lymphoid organ* containing predominantly unstimulated *B lymphocyte*s that develops into a *germinal center* following *antigen* stimulation.
[7]
See also *lymphoid follicle*.

primary lymphoid organ
Site at which *immunocompetent lymphocyte*s develop, i.e., *bone marrow* and *thymus* in mammals.
[3]

primary myxedema
Atrophic form of diffuse autoimmune thyroiditis.
See *thyroiditis, autoimmune*.
[1]

primary response
See *primary immune response*.

primary sclerosing cholangitis (PSC)
Chronic, non-bacterial, inflammatory narrowing of the bile ducts.
Note: Often associated with ulcerative colitis [see *inflammatory bowel disease (IBD)*].
After [1]

prime (vb)
Process of giving an initial *sensitization* to *antigen*.
[3]

priming
See *prime (vb)*.

privileged site
See *immunologically privileged site*.

professional antigen-presenting cell
Highly efficient *antigen-presenting cell (APC)*, generally referring to *dendritic cell*s, *B cell*s, or *macrophage*s.
Note: Other cells, e.g., *fibroblast*s and endothelial cells, that do not constitutively express *major histocompatibility complex (MHC) class II molecule*s may be induced to do so by certain *cytokine*s and are sometimes referred to as non-professional antigen-presenting cells.

programmed cell death
See *apoptosis*.

progressive systemic sclerosis
Systemic autoimmune disease marked by formation of hyalinized and thickened collagenous fibrous tissue, with thickening and adhesion of skin to underlying tissues, especially of the hands and face and vascular alterations.
See also *scleroderma*.

proinflammatory cytokine
Cytokine that initiates or enhances *inflammation*.

prolactin
Hormone that is involved in several aspects of endocrine physiology, including stimulation of milk production, which also regulates proliferation and differentiation of a variety of cells in the *immune system*.

Note: May play a role in the pathogenesis and clinical expression of *autoimmune disease*s [e.g., *systemic lupus erythematosus (SLE)*].

After [1]

proliferation assay
Any test that determines the effect on increase in cell number of a test agent such as a *cytokine* or *mitogen*.

properdin
Relatively heat-labile, normal *serum* protein (a *euglobulin*) that, in the presence of *complement* component C3 and magnesium ions, is involved in the *alternative pathway of complement activation*, and acts nonspecifically against gram-negative bacteria and viruses and may contribute to the lysis of *erythrocyte*s.

Note: It migrates as a β3-*globulin* and, although not an *antibody*, may act in conjunction with complement-fixing antibody.

prostaglandin
Acidic lipid derived from arachidonic acid that is able to increase vascular permeability, mediate fever, and can both stimulate and inhibit immunological responses.
[3]

proteasome
Cytoplasmic and nuclear multiprotein proteolytic complex involved in degradation of excess, damaged, or misfolded proteins.

Note: Cytoplasmic proteasome is important in *antigen processing and presentation* by *major histocompatibility complex (MHC) molecules*.

protectin
CD59
Member of the *Ly-6* family of cell surface molecules that prevents insertion of the *membrane attack complex (MAC)* into the membrane, thereby protecting cells from *complement*-induced lysis.

protective immunity
Protection against infectious agents conferred by *vaccination*.

protein A
Staphylococcus aureus cell wall protein that binds to the *Fc region* of *immunoglobulin G (IgG)*.

[3]

proteinase 3 (PR3)
Multifunctional enzyme of azurophilic granules of *neutrophil*s and *monocyte*s and the major target of *antineutrophil cytoplasmic autoantibodies (ANCA*).

Note: PR3 *autoantibodie*s are diagnostic markers for *Wegener granulomatosis (WG)* and are involved in the pathogenesis of this disease. They are also found in patients with other *autoimmune systemic* vasculitic diseases.

After [1]

protein G
Streptococcal cell wall protein that binds to the *Fc region* of *immunoglobulin G (IgG)*, with a wider species specificity than *protein A*.

protein kinase C (PKC)
Member of a kinase family with broad substrate specificity, activated by calcium, diacylglycerol, and (or) *phorbol myristate acetate (PMA)*.

Note: It is activated during *B lymphocyte* and *T lymphocyte* activation.

prozone effect
Loss of *immunoprecipitation* or *agglutination* that occurs when *antibody* concentration is increased to an extent that the antibody is in such excess that it is no longer able to effectively cross-link the *antigen*. A similar phenomenon may occur in antigen excess.
[3]

pseudoallergy
pseudoallergic reaction
Inflammatory or *anaphylactic* reaction with symptoms similar to an *allergy* but not involving an *antigen*-specific *immune response*, e.g., salicylate intolerance, reaction to contrast reagents.

Note: Causes include direct *histamine* release and (or) *complement* activation.

psoriasis
Skin disorder that has a hereditary component and is characterized by erythematous patches covered with silvery scales, especially on the elbows, knees, and scalp.

Note: Psoriasis is associated with excessively rapid proliferation of *keratinocyte*s which mature in less than a week.

psoriatic
Of, relating to, or associated with *psoriasis*; affected with psoriasis.

purified protein derivative (PPD)
Partially purified derivative of *tuberculin* used in the *Mantoux test* for tuberculosis.

purpura
Purple discoloration occurring in patches on the skin, mucus membranes, or organs.

See also *idiopathic thrombocytopenic purpura (ITP).*

pyrogen
Any substance that produces fever.
[5]

pyrogen test
Any of various tests used to determine whether an agent, usually an infusion or injection fluid, is free of *pyrogen*s.

Note: Examples include i) the rabbit test, observing whether the body temperature of the animal increases after administration of the agent, ii) the *Limulus test*, measuring the effects of *endotoxin*s on a biological system, and iii) in vitro tests, observing the release of *interleukin*-1β from human blood cells during incubation with the test fluid.

Qa antigen
'Non-classical' *major histocompatibility complex (MHC) class I molecule* in mice.
[3]

radial immunodiffusion
Mancini immunodiffusion
Method for quantifying an *antigen* by measuring the diameters of circular precipitates around an antigen-spiked cavity in an *antibody*-containing agar gel.

radioallergosorbent test (RAST)
Solid-phase *radioimmunoassay (RIA)* for detecting *immunoglobulin E (IgE) antibody* specific for a particular *antigen*.
[4]

radioimmunoassay (RIA)
Technique for measuring the level of a biologic substance in a sample, by measuring the binding of *antigen* to radioactively labeled *antibody* (or vice versa).
[7]

radioimmunoconjugate
Biochemical *conjugate* consisting of an immune-targeting molecule such as an *antibody* or antibody fragment together with a *cytotoxic* radionuclide.
[3]

Raynaud phenomenon
Intermittent bilateral attacks of vasospasm and ischemia of the fingers or toes and sometimes of the ears and nose, marked by a severe pallor and often accompanied by paresthesia and pain.

Note 1: It is brought on characteristically by cold or emotional stimuli and relieved by heat, and may be due to an underlying disease or anatomic abnormality.

Note 2: The phenomenon is more common in women than men and occurs in most

patients with *progressive systemic sclerosis (SSc)*, *mixed connective tissue disease (MCTD)*, and polymyositis/scleroderma overlap syndrome.

Note 3: When the condition is *idiopathic* or primary, it is termed Raynaud disease.

After [18]

reactive airways dysfunction syndrome (RADS)
Syndrome characterized by reversible airflow limitation and complicating bronchial hyperresponsiveness induced by acute exposure to high concentrations of non-*sensitizer* irritant gases.

reactive oxygen intermediate (ROI)
See *reactive oxygen species (ROS)*.

reactive oxygen species (ROS)
Intermediates in the reduction of molecular dioxygen, O_2, to water.

Note: Examples are superoxide ($O_2^{-\bullet}$), hydrogen peroxide (H_2O_2), and hydroxyl (HO•).

reagin
Historic term for *antibodies* of the *immunoglobulin E (IgE)* class.

recall antigen
Substance recognized by *memory cell*s that stimulates rapid *(secondary) immune response*s, often associated with *hypersensitivity*.

receptor
Molecule that binds to a *ligand*, thus leading to biochemical signaling inside the cell.

Note: Receptors are usually transmembrane molecules that bind ligands at the extracellular surface (e.g., *growth factor* receptors) or soluble intracellular molecules (e.g., steroid hormone receptors).

recombinant antibody
Antibody fragment manufactured by use of genetically modified microorganisms.

recombination-activating gene (RAG)
Gene whose products are involved in *V(D)J recombination* in *B cell*s and *T cell*s. Two such genes that have been identified are RAG-1 and RAG-2.

recombination signal sequence (RSS)
Any conserved heptamer (7- nucleotide)-nonamer (9-nucleotide) sequence, separated by a 12 or 23 base spacer, which occurs 3' of variable gene segments, 5' and 3' of diversity gene segments, and 5' of joining gene segments, in both *immunoglobulin (Ig)* and *T-cell receptor (TCR)* genes. It functions as a recognition sequence for the recombinase enzymes that mediate the gene rearrangement process involved in the generation of *lymphocyte antigen receptor* diversity.
After [3]

red pulp
splenic pulp
Parenchymal tissue of the *spleen* consisting of cords of cells and sinuses infiltrated with *erythrocyte*s and responsible for removal of aged or damaged erythrocytes.
See also *white pulp*.

Reed-Sternberg cell
Large transformed *lymphocyte*, often binucleate, considered pathognomonic of *Hodgkin lymphoma*.

regulated upon activation normal T cell expressed and secreted (RANTES)
Chemokine secreted by *T cell*s and *macrophage*s upon stimulation by *mitogen*s, which acts as a chemoattractant and stimulates *eosinophil*s and *basophil*s.

regulatory idiotope
Antibody or *T-cell receptor (TCR) idiotope* capable of regulating *immune response*s via interaction with *lymphocyte*s bearing complementary idiotopes (anti-idiotopes).
[3]

regulatory T cell (Treg)
T cell that controls the maintenance of normal immune homeostasis. Treg cells are involved in controlling (anergizing or counter-regulating) autoreactive cells that escaped from *thymic negative selection*.
See also *CD8+ T suppressor cell*, *CD4+CD25+ T cell*.
[1]

rejection (in immunology)
Immune response leading to destruction of a transplanted organ or tissue.
See also *acute rejection, chronic rejection, graft rejection*.

resistance (in immunology)
Ability of an organism to withstand an infection.
Note: Bacterial resistance is the ability of a bacterium to grow despite the presence of an antibiotic.

respiratory burst
Generation of *cytotoxic* superoxide from dioxygen due to increased NADPH oxidase activity, typically occurring in activated *neutrophils*.
See also *neutrophil activation*.

respiratory hypersensitivity assay
Test of the ability of a substance to induce *hyperreactivity* in the airways, typically measured as an increase in the rate of respiration of guinea pigs during inhalation of the substance.

restriction (in immunology)

See *major histocompatibility complex (MHC) restriction*.

reticuloendothelial system (RES)
See *mononuclear phagocyte system (MPS)*.

reverse immunology
High throughput procedure where information on potential *immunogen*ic tumor proteins is gained from the amino acid sequences of gene products specifically expressed by the tumor, followed by predicted fitting of putative *antigen*ic peptides to a *peptide-binding groove*, and finally experimental verification.

Rhesus (Rh) **factor**
Protein expressed on the surface of *erythrocyte*s, especially the D *antigen* of the Rh *blood group*.

Note: Rh positivity is a common cause of *transfusion* reaction and hemolytic disease of the newborn.

rheumatic fever
Inflammatory disease that may develop following a streptococcal infection such as strep throat, and may affect the heart, joints, skin, and brain.

rheumatoid arthritis (RA)
Episodic inflammatory *systemic* disease with *autoimmune* pathogenetic mechanisms.

Note: It primarily affects the joints, causing symmetrical lesions and severe damage to the affected joints. RA is the most common form of inflammatory joint disease (prevalence about 0.5–1%).

After [1]

rheumatoid factor
*Immunoglobulin*s *IgM*, *IgG* and *IgA autoantibodies* to the *Fc region* of IgG.

Note: Although detectable in various diseases, rheumatoid factor is used as a classification criterion of *rheumatoid arthritis (RA)*.

Modified from [3]

rhinitis
Inflammation of the mucous membrane of the nose.

rhinitis, allergic
Nasal discharge resulting from an *allergic* response.

rocket electrophoresis
Technique in which a test *antigen* is electrophoretically driven through an *antibody*-containing gel. The rocket-shaped tails of precipitation give information on the antigen concentration.

rosette

Particles or cells bound to the surface of a *lymphocyte* (e.g., sheep *erythrocyte*s around a human *T cell*).
[3]

scFv
Single chain molecule composed of the *variable (V) region*s of an *antibody heavy* and *light chain* joined together by a flexible linker.
[3]

sarcoid
See *sarcoidosis*.

sarcoidosis
Chronic, progressive, generalized *granuloma*tous reticulosis of unknown etiology, involving almost any organ or tissue, including the skin, lungs, lymph nodes, liver, spleen, eyes, and small bones of the hands and feet. It is characterized histologically by the presence in all affected organs or tissues of noncaseating epithelioid cell tubercles.

Note: There is usually diminished or absent reactivity to *tuberculin*, and in most active cases, a positive *Kveim reaction*.

scavenger receptor
Cell surface *receptor*, for example on *phagocytes*, which recognizes cells or molecules that require clearance from the body.
[3]

scleroderma
Chronic progressive *autoimmune disease* characterized by systemic fibrosis and vascular changes.

Note: There are two types: *progressive systemic sclerosis*, and a more limited and less rapidly progressive form known as CREST syndrome, referring to **C**alcinosis, ***R**aynaud phenomenon*, **E**sophageal dysfunction, **S**clerodactyly, and **T**elangiectasias.

secondary challenge
Second exposure of *prime*d *lymphocyte*s to a given *antigen*.
See also *secondary immune response.*

secondary immune response
Qualitatively and quantitatively improved *immune response* that occurs upon the second encounter of *prime*d *lymphocyte*s with a given *antigen*.
[3]

secondary lymphoid tissue (organ)
Tissue (organ) in which *antigen*-driven proliferation and differentiation of *mature B* and *T lymphocyte*s take place following antigen recognition. Examples include *lymph node*s, *Peyer's patch*es, and the *spleen*.

See also *mucosa-associated lymphoid tissue (MALT)*.
[7]

second messenger
Substance inside a cell responsible for communicating a chemical signal from another substance that cannot itself enter the cell, but acts through binding to cell surface *receptor*s.

Note: Common second messengers are cyclic AMP, Ca^{2+}, and inositol-1,4,5-triphosphate.

second set rejection
Accelerated *rejection* of an *allograft* in a *prime*d recipient.
[7]

secretory component
Proteolytic cleavage product of the *poly-Ig receptor* which remains associated with dimeric *immunoglobulin A (IgA)* in sero-mucus secretions.
[3]

secretory immunoglobulin A (IgA)
Dimeric *immunoglobulin A (IgA)* found in sero-mucus secretions.
[3]

selectin
Any member of a family of cell-surface *adhesion molecule*s found on *leukocyte*s and endothelial cells and that bind to sugars on glycoproteins.

selection theory (in immunology)
See *clonal selection*.

selective IgA deficiency (SIgAD)
Most common form of primary *immunodeficiency*.

Note: *Autoimmunity* is the most prevalent manifestation of this deficiency. Individuals with SIgAD have an increased risk of developing *systemic* [e.g., *systemic lupus erythematosus (SLE)*, *rheumatoid arthritis (RA)*] and organ-specific (e.g., *celiac disease*) *autoimmune* disorders.

After [1]

self-antigen
See *autoantigen*.

self-tolerance
Specific immunological unresponsiveness to a defined *autoantigen*.

Note 1: Primary (*clonal deletion*, *anergy*, *clonal indifference*) and secondary or regulatory (interclonal competition, suppression, *immune deviation*, *vetoing*, feedback regulation by the *idiotypic network*) mechanisms are involved in

the induction and maintenance of self-tolerance.

Note 2: Breaking self-tolerance may lead to pathological *autoimmunity* and development of *autoimmune disease*.

After [1]

sensitization
Alteration of a body's responsiveness to a foreign *antigen*, usually an *allergen*, such that upon subsequent exposures to the allergen there is a heightened *immune response*.

sensitizer
Substance that brings about *sensitization*.

sepsis
Spread of bacteria or bacterial products throughout the blood, eliciting a life-threatening, *systemic* inflammatory reaction (see *inflammation*).

seroconversion
The appearance in the blood *serum* of detectable *antibodies* against a specific infectious agent.

serology
Study of *serum*, especially blood serum, frequently used to detect *antibodies* to microorganisms.

serum
1. Clear watery fluid, especially that which moistens the surface of serous membranes or that exudes through *inflammation* of any of these membranes.
2. Watery proteinaceous portion of the blood that remains after clotting.
[5]

serum sickness
Hypersensitive reaction to the administration of a foreign *serum*, characterized by fever, swelling, skin rash, and enlargement of the *lymph node*s.

severe combined immunodeficiency (SCID)
Immunodeficiency affecting both *T* and *B lymphocyte*s.
[3]

sheep red blood cell (SRBC) **antigen**
T cell-dependent target *antigen* often used in hemolytic plaque assays of *immune responsiveness*.

signaling lectin (SIGLEC)
Any member of a large family of *lectins* that bind sialylated glycans.

Note: Most are associated with cells of the *immune system*.

signal peptide
signal sequence
Any sequence of amino acid residues that, when linked to a newly synthesized protein, identifies it to transport mechanisms that guide the protein to a specific location among the organelles of a eukaryotic cell, or from the cytoplasm to the periplasmic space of prokaryotic cells.

signal sequence
See *signal peptide*.

signal transducer and activator of transcription (STAT)
Any member of a family of cytoplasmic proteins that act as *second messenger*s to activate gene transcription in response to *cytokine*s and *growth factor*s.
See also *JAK/STAT signaling pathway*.

signal transduction
Process whereby a signal arising outside the cell is converted through a series of intermediate chemical reactions inside the cell to produce a functional change in the cell.
See also *cytokine, growth factor*, *receptor*, *second messenger*.

single-chain antibody (SCA)
Small *antibody* construct in which the variable fragment (*Fv*) [see *variable (V) region*] of a *heavy chain* is linked via a synthetic peptide to the variable fragment of a *light chain*.

single-nucleotide polymorphism (SNP)
Single base variation at a chromosomal locus, which exists stably within populations (typically defined as each variant form being present in at least 1–2 % of individuals).
[5]

single-positive cell
See *pre-T cell.*

Sjögren syndrome
Chronic *inflammation* of the lachrymal and salivary glands, often accompanied by *rheumatoid arthritis (RA)* and the presence of *autoantibodies* in the blood, occurring chiefly among women.

Note: Two types of Sjögren syndrome are distinguished: a primary (isolated) type and a secondary type associated with another underlying autoimmune disease [e.g., *RA*, *systemic lupus erythematosus (SLE)*, *systemic sclerosis (SSc)*, *primary biliary cirrhosis (PBC)*, *autoimmune hepatitis (AIH)*, *multiple sclerosis*, *autoimmune thyroiditis*, etc.]. Ro/SS-A and La/SS-B autoantibodies are used as classification criteria.

Modified from [1]

skin immune system (SIS)
Skin-associated cells that participate in an *immune response*, including *Langerhans*

*cell*s, *dendritic cell*s, and *keratinocyte*s (mainly responsible for production of *cytokine*s). [8]

skin sensitization test
Any test used to study skin *hypersensitivity* such as the *guinea pig maximization test* or the *Buehler test*.

skin test
Procedure for evaluating *immunity* status, involving the introduction of a reagent into or under the skin.

slow-reacting substance of anaphylaxis (SRS-A)
Group of *leukotriene*s released by *mast cell*s during *anaphylaxis*, which induces a prolonged contraction of smooth muscle.
After [7]

small G protein
Any member of a family of monomeric *G protein*s, with molecular mass typically 20-40 kDa, that also bind guanine nucleotides and are involved in *signal transduction*.

small outer capsid (SOC) **protein**
Protein from the shell of the bacteriophage T4, commonly used in construction of *phage antibody libraries*.

somatic diversification theory
Theory that very few *immunoglobulin*s *(Ig)* are inherited, but that extensive *antibody* diversity arises from mutations in non-reproductive cells.
See also *somatic hypermutation*, *somatic recombination*, *V(D)J recombination*.

somatic gene conversion
Nonreciprocal exchange of nucleic acid sequences between genes in which part of the donor gene or genes is "copied" into an acceptor gene, but only the acceptor gene is altered.
Note: This exchange is a mechanism for generating a diverse *immunoglobulin (Ig)* repertoire in many non-human species.
After [7]

somatic hypermutation (SHM)
Programmed process of mutation affecting the *variable (V) region*s of *immunoglobulin (Ig)* genes. SHM affects only individual immune cells, and the mutations are not transmitted to offspring.
Note 1: This process is part of the way the *immune system* adapts to new foreign substances.
Note 2: Mistargeted SMH is a likely mechanism in the development of B-cell *lymphoma*.

somatic recombination
Process giving rise to increased *antibody* diversity by cutting and splicing *immunoglobulin (Ig)* genes during *lymphocyte* differentiation.
See also *combinatorial diversity*, *V(D)J recombination*.

spleen
Largest of the *secondary lymphoid organ*s, composed of *white pulp*, rich in lymphoid cells, and *red pulp*, which contains many *erythrocyte*s and *macrophage*s.
Note: The spleen traps damaged erythrocytes carried in the blood.
After [7]

splenic
Of, pertaining to, connected with, or situated in the *spleen*.

splenic pulp
See *red pulp*.

splenocyte
Any *splenic* cell.

split adjuvant technique
Test for *allergic contact dermatitis* in which Guinea pig skin is exposed to repeated applications of a test substance and intradermal injections of complete *Freund's adjuvant* are administered separately.

spondylitis
Inflammation of the vertebral column.

spontaneous autoimmune thyroiditis (SAT)
Autoimmune thyroiditis *(*see *thyroiditis, autoimmune*) that develops spontaneously (without any apparent cause or manipulation) in certain strains of mice and rats (e.g., *NOD mice*, BB and BUF rats) as well as in other animals (e.g., OS chickens, marmoset monkeys, beagles).
[1]

stem cell
Multipotent cell with mitotic potential that may serve as a precursor for many kinds of differentiated cells.
[5]

Stevens-Johnson syndrome
bullous erythema multiforme
Allergic reaction, often to a medication (see *adverse drug reaction*) or infection, characterized by blistering of the skin and ulceration of *mucosa*l membranes.

stroma

Supporting tissue of an organ.

stromal cell
Cell found in the loose connective tissue (*stroma*) of an organ. Stromal cells include immune and inflammatory cells, pericytes, and *fibroblast*s.

subacute cutaneous lupus erythematosus (SCLE)
Chronic remitting form of *dermatitis* characterized by severe photosensitivity and Ro/SS-A and La/SS-B *autoantibodies*.
[1]

superantigen
Antigen which reacts with all the *T cell*s belonging to a particular *T-cell receptor (TCR) variable (V) region* family, and which therefore stimulates (or deletes) a much larger number of cells than does conventional antigen.
[3]

superfamily
Large group of proteins related by structural homology and function. The term also refers to the genes that encode them.

suppression
Dominant immunological *tolerance*, a phenomenon that plays an active role in regulating *T cell* and *B cell* responses to both foreign *antigen*s and *autoantigen*s.
Note: The downregulation of responses to autoantigens is a major regulatory mechanism involved in the induction and maintenance of *self-tolerance*.
After [1]

suppressor cell
suppressor T cell
suppressor T lymphocyte
T cell that suppresses the *immune response* of *B cell*s and other T cells to an *antigen*. In more current usage classified as a *regulatory T cell*.

supramolecular adhesion complex (SMAC)
Collection of molecules forming at the contact point of a *T cell* and an *antigen-presenting cell (APC)*, enriched in *T-cell receptor (TCR)*, *adhesion molecule*s, and signaling molecules.

surrogate light chain
Light chain-like structure formed when the proteins encoded by the V_{preB} and λ_5 genes associate with each other. It can form *immunoglobulin (Ig)*-like complexes which are expressed on the surface of *pre-B cell*s at different stages of development.
After [29]

switch region

See *switch sequence*.

switch sequence
Highly conserved repetitive sequence that mediates *class switching* in the *immunoglobulin (Ig) heavy chain* gene locus.
[3]

sympathetic ophthalmia
Autoimmune injury to one eye that occurs after penetrating injury or surgery to the other eye.

syngeneic
Genetically identical, e.g., a fully inbred strain of mice.
[3]
Note: A practical consequence is that cells can be transferred to other syngeneic animals without *rejection*.

syngraft
See *isograft*.

systemic
1. Relating to the body as a whole.
2. Occurring at a site in the body remote from the point of contact with a substance.
[5]

systemic autoimmune disease
Autoimmune disease affecting a number of organs or tissues, or the whole body.

systemic lupus erythematosus (SLE)
Chronic *autoimmune disease* that is potentially debilitating and sometimes fatal as the *immune system* attacks the body's cells and tissues, with *inflammation* and tissue damage.
Note 1: SLE can affect any part of the body, but most often harms the heart, joints, skin, lungs, blood vessels, liver, kidneys and nervous system. The course of the disease is unpredictable, with periods of illness (called flares) alternating with remission. SLE can occur at any age, and is most common in women, particularly of non-European descent.
Note 2: The disease is very heterogeneous in clinical expression and serological factors. *Autoantibodies* directed against nuclear components [*antinuclear antibodies (ANA)*] are typically detected. Anti-dsDNA, anti-Sm, and antiphospholipid *antibodies* are used as classification criteria.
Modified from [1]

systemic sclerosis (SSc)
Fibrosing disease of unclear etiology that affects multiple organ systems.
Note 1: The skin ("*scleroderma*") and blood vessels (arteries, small vessels) are

most commonly affected, but involvement of the lungs and gastrointestinal tract (esophagus) may also be observed.

Note 2: Anticentromere *antibodies* (ACA) as well as *autoantibodies* against DNA topoisomerase I (scl-70) and various nucleolar *antigens* are diagnostic and prognostic markers and are often detectable years before disease manifestation. They are also detectable in quartz dust-exposed individuals.

After [1]

T cell
See *T lymphocyte*.

T cell, drug-specific
T-*memory cell* that is specific for a drug *allergen*.

T cell-dependent antibody response (TDAR)
*Immunotoxic*ity test that evaluates the ability of animals to produce *antibodies* to a *T-dependent antigen* [e.g., *sheep red blood cells (SRBC)* or *keyhole limpet hemocyanin (KLH)*].

T-cell receptor (TCR)
Antigen-specific *receptor* on *T cells* composed of one set of heterodimeric chains. Two types of TCR heterodimers are known (α/β and γ/δ).

Note: Functional binding for TCR requires a complex of *major histocompatibility complex (MHC) molecule*, *antigenic* peptide, and TCR.

After [1]

T-dependent antigen
Antigen which requires *helper T lymphocytes (Th)* in order to elicit an *antibody* response.
[3]

TdT-dependent dUTP-biotin nick end labeling (TUNEL) **assay**
Method for detecting *apoptotic* cells in situ based on characteristic DNA fragmentation. It is based on the ability of *terminal deoxynucleotidyl transferase (TdT)* to transfer a labeled deoxyuridine triphosphate to the terminal ends arising from DNA cleavage.

T helper cell
See *helper T lymphocyte (Th)*.

Th0 cell
Helper T lymphocyte (Th) with a less restricted *cytokine* profile than *Th1* and *Th2 cells*.

Note: Th0-like responses are observed in patients with *rheumatoid arthritis (RA)*, *Sjögren syndrome*, and *Graves disease*.

After [1]

Th1 cell

Helper T lymphocyte (Th) producing mainly *interleukin*-2 (IL-2), *interferon (IFN-γ)*, and *tumor necrosis factor β (TNF-β)*, and thereby responsible for *phagocyte*-dependent *host* responses.

Note: Th1-dominated responses are seen in *autoimmune disease*s in which *cytotoxic T cell*s and *macrophage*s play a major role, e.g., *multiple sclerosis*, *diabetes mellitus type 1*, *Hashimoto thyroiditis*, and *Crohn disease*. Switching from Th1 to *Th2* response can prevent Th1-mediated tissue destruction in animal models.

After [1]

Th2 cell
Helper T lymphocyte (Th) in mice producing *interleukin*s IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13.

Note: Besides other effects, they provide optimal help for *antibody* responses. Th2 responses should also be regarded as an important downregulatory mechanism for exaggerated *Th1* responses. Predominant Th2 *cytokine* profile is observed in patients with *atopic* disorders and *graft-versus-host disease (GVHD)*.

After [1]

Th3 cell
Helper T lymphocyte (Th) producing and responding to *transforming growth factor β (TGF-β)* and helping *immunoglobulin A (IgA) antibody* responses.

Th9 cell
Helper T lymphocyte (Th) producing *interleukin* IL-9, which stimulates *mast cell*s.

Th17 cell (T17)
Helper T lymphocyte (Th), distinct from *Th1* and *Th2 cell*s, that secretes the *interleukin* IL-17.

Note: T17 *lymphocyte*s are thought to play an important role in *autoimmune disease*.

T-independent antigen
Antigen that is able to elicit an *antibody* response in the absence of *T cell*s.
[3]

T lymphocyte
Lymphocyte that matures in the *thymus* and has the ability to recognize specific peptide *antigen*s through the *receptor*s on its cell surface.
Note: T-cell receptor (TCR) molecules are specific for complexes comprising short peptides bound to and presented by *major histocompatibility complex (MHC) molecule*s.

Tr1 cell
T lymphocyte that regulates *Th1 cell* responses. It resembles the *regulatory T cell (Treg)* and is possibly related to the *Th3 cell*.

Note: It is abundant in the intestine and may be involved in *tolerance* to dietary *antigen*s.

tandem conjugate
Molecular construct with two fluorochromes where the first excites the second by its emission.
Note: Used in *flow cytometry* analysis.

target cell (in immunology)
Cell killed by one of the body's *killer cell*s, such as a *cytotoxic T lymphocyte* or *natural killer (NK) cell*.

terminal deoxynucleotidyl transferase (TdT)
Enzyme that inserts non-coded nucleotides at the junctions of *V*, *D*, and *J gene* segments of *immunoglogulin (Ig)* and *T-cell receptor (TCR)* locus DNA, thus increasing the diversity of *antigen*-specific recognition.

tetanus toxoid
Detoxified tetanus *toxin* used to produce active immunity (see *active immune response*) against tetanus.

tetradecanoyl phorbol acetate (TPA)
See *phorbol myristate acetate (PMA)*.

tetramer staining
Technique used for selective staining of *antigen*-specific *T-lymphocyte*s in vitro or in situ. The antigen is presented to T-cells by *peptide tetramer* constructs of *major histocompatability (MHC) class I molecule*s. It is also used to isolate antigen-specific T-cell populations for *clonal expansion*.

tertiary lymphoid tissue (organ)
Ectopic lymphoid aggregates that accumulate during the process of chronic immune stimulation, and exhibit characteristics usually associated with the *secondary lymphoid organ*s.
[30]

therapeutic antibody
See *antibody, therapeutic*.

thrombocyte
Same as *platelet*.

thrombocytopenia
Abnormal decrease in the number of *platelet*s to <150 x 10^9/L of blood.
Note: Frequently detected in patients with *autoimmune disease*s [e.g., *systemic lupus erythematosus (SLE)*, *Sjögren syndrome*, *mixed connective tissue*

disease (MCTD), *antiphospholipid syndrome (APS)*]. Primary forms may be drug-induced (heparin-induced thrombocytopenia) or mediated by antiplatelet *antibodies* [*idiopathic thrombocytopenic purpura (ITP)*].

After [1]

thromboxane
Any of several substances (predominantly thromboxanes A2 and B2) synthesized by *platelet*s from arachidonic acid precursor, that cause vasoconstriction of vascular and bronchial smooth muscle and facilitates platelet aggregation.

thrush
Oral infection with Candida albicans, often in patients with *immunosuppression*.

thymic
Pertaining to the *thymus*.

thymic atrophy
Involution of the *thymus* gland leading to a diminished capacity to generate new *T cell*s.

thymic education
Process by which *T cell*s, developing in the *thymus*, are screened for potentially harmful self-reactive T cells (which are removed), while potentially beneficial T cells are promoted.

thymocyte
See *pre-T cell*.

thymoma
Rare, usually benign, tumor arising from tissue of the *thymus* gland.

Note: Thymoma is often associated with *myasthenia gravis*.

thymus
Pyramid-shaped organ in the thoracic or cervical region of mammals, composed of *lymphatic tissue* in which minute concentric bodies (*thymic* corpuscles, the remnants of epithelial structures) are found.

*Note 1: Stem cell*s in the outer cortex of thymus develop into different kinds of *T cell*s. Some migrate to the inner *medulla* and enter the bloodstream; those that do not may be destroyed to prevent *autoimmune* reactions.

Note 2: This organ is necessary for the development of thymus-derived *lymphocyte*s (T cells) and is the source of several hormones involved in T cell maturation, for example, thymosin, thymopoietin, thymulin, and thymocyte humoral factor.

Note 3: If a newborn's thymus is removed, not enough T cells are produced, the *spleen* and *lymph node*s have little tissue, and the *immune system* fails, causing a gradual, fatal wasting disease. Thymus removal in adults has little effect.

thymus-dependent (TD) **antigen**
Antigen that requires the participation of *T lymphocyte*s to elicit an *immune response* in *B lymphocyte*s.

thymus-independent antigen
Antigen that does not require the participation of *T lymphocyte*s to elicit an *immune response* in *B cell*s.

thyroglobulin (TG)
Glycoprotein secreted by thyroid follicular cells that is a major *autoantigen* in *autoimmune disease*s of the thyroid.
Note: Thyroglobulin *autoantibodies* are found in patients with *autoimmune thyroiditis*, and *Graves disease*.
After [1]

thyroiditis, autoimmune
Inflammatory destruction of the thyroid gland (ranging from a mild focal thyroiditis to extensive *lymphocytic* infiltration and scarring) often associated with goitre and hypothyroidism.
Note: The most common types of autoimmune thyroiditis are *Hashimoto thyroiditis* and atrophic thyroiditis.
After [1]

thyroid-stimulating hormone receptor (TSHR)
Main *autoantigen*ic target in patients with *Graves disease*.
Note: Most TSHR *autoantibodies* are stimulatory, acting as agonists of thyroid-stimulating hormone, but *receptor*-blocking *antibodies* are also found.
After [1]

thyroid peroxidase (TPO)
Thyroid enzyme that is a major *autoantigen* in *autoimmune disease*s of the thyroid.
[1]

tissue transglutaminase (tTG)
Main target of *autoantibodies* in *celiac disease*.
[1]

titer (in immunology)
Reciprocal of the highest dilution of a titration of an *antigen* with an *antibody* that gives a measurable effect (e.g., *agglutination*), and thus an empirical measure of the *avidity* of an antibody. For example, if the effect is seen until a dilution of 1:1000, the antibody titer is 1000.

tolerance
See *immunological tolerance*.

tolerogen
Antigen used to induce *tolerance*.
Note: Induction depends strongly on the circumstances of administration (e.g., route and concentration) in addition to any inherent property of the molecule.
After [3]

Toll-like receptor (TLR)
Member of a family of *pattern recognition receptor*s involved in the detection of structures associated with pathogens or damaged *host* tissues.

tonsil
Small, rounded mass of tissue, especially of *lymphoid tissue*; generally used alone to designate one of the paired palatine tonsils.

toxic epidermal necrolysis (TEN)
Lyell syndrome
A severe form of *Stevens-Johnson syndrome* with extensive detachment of the skin, often as a result of an *allergic adverse drug reaction*.

toxic shock syndrome
Systemic reaction produced by the *toxin* derived from the bacterium Staphylococcus aureus; the toxin acts as a *superantigen*, which activates a high proportion of *CD4+ T lymphocyte*s to produce *cytokine*s.
[7]

toxin
Poisonous substance produced by a biological organism such as a microbe, animal, plant, or fungus.
Note: Examples are botulinum toxin, tetrodotoxin, pyrrolizidine alkaloids, and amanitin.
[5]
Compare *immunotoxin*.

toxoid
Chemically or physically modified *toxin* that is no longer harmful but retains *immunogen*icity.
[3]

transcytosis
Vesicular transport of macromolecules from one side of a cell to the other, through the cell's interior.

transforming growth factor β (TGF-β)
Secreted member of the protein *superfamily* of the same name that functions in

controlling the cell cycle and *apoptosis*.

Note: TGF-β is involved in several aspects of regulation of the *immune system* and blocks activation of *lymphocyte*s and *macrophage*s.

transfusion, blood
Transference of blood or blood-based products from one individual into the circulation of another.

transplantation
Grafting solid tissue (e.g., cornea) or organ (e.g., kidney or heart), or cells (particularly *bone marrow*), from one individual to another.
See also *allograft*, *xenograft*.
After [7]

transplant rejection
See *rejection*.

transporters associated with antigen processing (TAP-1 and TAP-2)
Molecules that carry *antigenic* peptides from the cytoplasm into the lumen of the endoplasmic reticulum for incorporation into *major histocompatibility (MHC) class I molecule*s.
[3]

tryptophan
(2S)-2-amino-3-(1H-indol-3-yl)propanoic acid
Essential amino acid for humans, and required for *T cell* proliferation.
See also *indolamine-2,3-dioxygenase (IDO)*.

tuberculin
Antigen found in extracts of Mycobacteria, used in a *skin test* for tuberculosis *(Mantoux test).*

tuberculin test
Diagnostic test in which *antigen*s derived from the organism causing tuberculosis (Mycobacterium tuberculosis) are injected subcutaneously; individuals who have been exposed to the organism develop a *delayed-type hypersensitivity (DTH)* response at the injection site 24-48 hours later.

Note: those who have been previously vaccinated with *bacille Calmette–Guérin (BCG)* also show a positive response.

[7]

tumor antigen
Antigen whose expression is associated with tumor cells.
[3]

tumor immunology

Application of *immunology* to understanding tumor biology, *immune system* avoidance by tumors, and *immunotherapy* directed against tumors.

tumor-infiltrating lymphocyte (TIL)
Mononuclear *lymphocyte* derived from the inflammatory infiltrate of a solid tumor.
After [7]

tumor necrosis factor (TNF)
cachectin
cachexin
TNF-α
Protein produced and secreted by several of the body's cell types, including *leukocyte*s.

Note 1: It promotes the destruction of some types of cancer cells and is a *cytokine* involved in *systemic inflammation*.

Note 2: Activation of the TNF-α *receptor* may trigger *apoptosis* through the *extrinsic pathway*.

After [5]

tumor necrosis factor β (TNF-β)
See *lymphotoxin.*

tumor necrosis factor (TNF) **receptor-associated factor** (TRAF)
Family of proteins involved in regulating *inflammation* and *apoptosis* through interaction with the *tumor necrosis factor receptor*.

tumor rejection antigen (TRA)
Antigen present specifically on a tumor cell that may target it for destruction by the *immune system* or for *antibody therapy*.

tumor-specific transplantation antigen (TSTA)
Any of several *antigen*s uniquely expressed by certain tumor cells, detected by production of *antibodies* or *T lymphocyte*s following tumor transplantation (e.g., in mice).

type 1 diabetes mellitus
See *diabetes mellitus type 1*

type I hypersensitivity
See *Gell and Coombs classification*, *immediate-type hypersensitivity*.

type II hypersensitivity
See *Gell and Coombs classification*.

type III hypersensitivity
See *Gell and Coombs classification*.

type IV hypersensitivity

See *Gell and Coombs classification*.

tyrosine kinase
protein tyrosine kinase
Any member of a family of enzymes that phosphorylates target proteins on tyrosine residues, thus playing a crucial role in *signal transduction*.

Note: Tyrosine kinases play a key role in *lymphocyte activation*. Major tyrosine kinases involved in *T lymphocyte* activation are Lck, Fyn, and *ZAP-70*; those involved in *B lymphocyte* activation are Blk, Fyn, Lyn, and Syk.

After [7]

ubiquitin
Highly conserved 76 amino acid peptide abundant in eukaryotic cells. Its covalent attachment to a protein by a ubiquitin ligase complex targets that protein for destruction by the *proteasome*.

unresponsiveness (in immunology)
Inability to respond to an *antigen*ic stimulus.

Note: Unresponsiveness may be specific for a particular antigen (see *tolerance*), or broadly nonspecific as a result of damage to the entire *immune system*, for example, after whole-body irradiation.

After [7]

urticaria
See *hives*.

Vα-Jα rearrangement
Preferential partnering of Jα gene segments with Vα gene segments during rearrangement in the *T-cell receptor (TCR)* gene, possibly following deletion of the Vδ gene region.

V(D)J recombination
Mechanism for generating *antigen*-specific *receptor*s of *T cells* and *B cell*s; it involves the joining of *V*, *D*, and *J gene* segments, mediated by the enzyme complex V(D)J recombinase, and products of the *recombination-activating gene*s.
[7]

Note 1: The conventional syntax V(D)J indicates that V and J genes code the *light chain* and all three genes code the *heavy chain*, the processes being VJ and VDJ recombination, respectively.

Note 2: Recombination occurs only once in a cell's lifetime.

See also *somatic recombination*.

V domain
See *variable (V) region*.

V gene

See *variable (V) gene*.

V region
See *variable (V) region*.

vaccination
Immunization with a *vaccine* against a pathogen.

vaccine
Preparation of an *antigen* intended to stimulate the *immune system* to render future *tolerance*, often of a weakened or killed pathogen, such as a bacterium or virus, or of a portion of the pathogen's structure. Upon administration the vaccine stimulates *antibody* production or *cellular immunity* against the pathogen but is incapable of causing severe infection.
See also *attenuated vaccine*, *inactivated vaccine*.

variable (V) domain
See *variable (V) region*.

variable (V) gene
Gene, segment(s) of which rearrange together with *diversity (D) gene* and *joining (J) gene* segments in order to encode the *variable (V) region* amino acid sequences of *immunoglobulin*s *(Ig)* and *T-cell receptor*s *(TCR)*.
[3]
See also *variable (V) region*.

variable (V) region
N-terminal portion of an *immunoglobulin (Ig)* or *T-cell receptor (TCR)* that contains the *antigen*-binding region of the molecule. V regions are formed by the recombination of V(D) and *J gene* segments.
Note: The V region consists of two V domains, V_L and V_H.
[7]
See also *somatic recombination, V(D)J-recombination*.

vascular addressin
Cell *adhesion molecule* present on the luminal surface of blood and *lymph* vessel endothelium, recognized by *homing* molecules thatr direct *leukocyte*s to tissues with the appropriate 'address'.
[3]

vascular cell adhesion molecule (VCAM)
CD106
Molecule, expressed on the surface of endothelial cells that functions in the adhesion of *lymphocyte*s, *monocyte*s, *eosinophil*s, and *basophil*s to vascular endothelium to the vascular surface.
See also *adhesion molecule*.

vasculitis
Group of disorders that share a common underlying problem of *inflammation* of a blood vessel or vessels.

Note: Vasculitis can lead to *necrosis*, fibrosis, or thrombosis. *Autoimmunity* plays an important role in some vasculitides (e.g., *ANCA-associated vasculitides*, *Goodpasture syndrome*, *cryoglobulinemic vasculitis*).

After [1]

vasoactive amine
Substance containing amino group(s) that increases vascular permeability and smooth muscle contraction. Examples are *histamine* and 5-hydroxytryptamine.

very early activating antigen
CD69
Specific *antigen* expressed on *lymphocyte*s very soon after *activation* by *phorbol myristate acetate (PMA)*.

very late activation antigen (VLA)
T cell surface *antigen*, named for its delayed appearance after *T cell* activation; a member of the *integrin superfamily* involved in cell adhesion.

vetoing
Elimination by *apoptosis* of a self-peptide-*major histocompatibility complex (MHC) molecule* recognizing *lymphocyte* by a self-peptide-presenting (veto) cell.
After [1]

warm autoantibody type
Autoantibodies that react optimally at higher temperatures (37 °C) with surface *antigen*s of *erythrocyte*s. They mediate *autoimmune hemolytic anemia*.
[1]

Wegener granulomatosis (WG)
*Granuloma*tous *inflammation* involving the respiratory tract, and necrotizing *vasculitis* affecting small to medium-sized vessels (e.g., capillaries, venules, arterioles, and arteries).

Note: Necrotizing *glomerulonephritis* is common in WG.

[1]

western blotting
See *immunoblotting*.

wheal
Circumscribed papule or plaque of *edema* of the skin, occurring as an *urticaria*l lesion. See also *hives*.

After [9]

wheal and flare
Dermatological reaction at a skin site where an *antigen* is injected into an *allergic* individual. The reaction is characterized by a "flare" of *erythema* and a *wheal* produced by *serum* exuding into tissue, causing local *edema*.

white pulp
Collections of *lymphocyte*s in the *spleen*, responsible for its *immune* function.
See also *red pulp*.

Wiskott-Aldrich syndrome
eczema-thrombocytopenia-immunodeficiency syndrome
Condition characterized by chronic *eczema*, chronic suppurative otitis media, *anemia*, and *thrombocytopenic purpura* (accompanied by bloody diarrhea); it is an *immunodeficiency* syndrome transmitted as an X-linked recessive trait, in which there is poor *antibody* response to polysaccharide *antigen*s and dysfunction of *cell-mediated immunity*.
After [18]

X-linked agammaglobulinemia
Bruton Syndrome
Sex-linked impairment of the ability to produce *mature B cell*s, thus characterized by recurrent infections.

X-linked severe combined immunodeficiency
Sex-linked trait carried on the X-chromosome of *severe combined immunodeficiency* syndrome resulting from nonfunctional *B lymphocyte*s and lack of *T lymphocyte*s and *natural killer (NK) lymphocyte*s, leading to recurrent, persistent, and severe infections.

xenobiotic
Substance with a chemical structure foreign to a given organism.
Note: Frequently restricted to man-made substances.
[5]

xenogeneic
Exhibiting genetic differences between species.
After [3]

xenograft
Tissue or organ *graft* between individuals of different species.
[3]

xenophagy
Autophagy selective for degradation of intracellular bacteria and viruses.

Zeta chain (TCR)-associated protein kinase-70 kDa (ZAP-70A)

T lymphocyte-specific *tyrosine kinase* involved in T lymphocyte *activation*.

zymosan

Crude preparation of yeast cell walls, consisting chiefly of polysaccharide, activating the *alternative pathway* of the *complement system* in the presence of *properdin* and used in the immunoassay of this compound.

REFERENCES FOR ALPHABETICAL ENTRIES

1. IPCS, Principles and Methods for Assessing Autoimmunity. Environmental Health Criteria. Vol. 236. 2006, Geneva: World Health Organization.

2. Murphy, K., Travers, P., Walport, M., and Janeway Jr, C.A., Janeway's Immunobiology, 7th Ed. 2008, New York: Garland Science.

3. Delves, P.J., Martin, S., Burton, D., and Roitt, I., Roitt's Essential Immunology, 11th Revised Ed. 2006, Oxford: John Wiley and Sons & Blackwell Publishing.

4. IPCS, Principles and Methods/Assessing Allergic Hypersensitization Associated with Exposure to Chemicals. Environmental Health Criteria. Vol. 212. 1999, Geneva: World Health Organization.

5. Duffus, J.H., Nordberg, M., and Templeton, D.M., Glossary of terms used in toxicology, 2nd Ed. Pure Appl. Chem., 79: 1153-1341 (2007).

6. Edwards, I.R. and Aronson, A.K., Adverse drug reactions: definitions, diagnosis, and management. Lancet, 356: 1255-1259 (2000).

7. Benjamini, E., Coico, R., and Sunshine, G., Immunology, A Short Course, 4th Ed. 2000, Oxford: Wiley Interscience.

8. Thomas, P.T. and House, R.V., Chapter 7. Preclinical Immunotoxicity Assessment, in CRC Handbook of Toxicology, M.J. Derelanko and M.A. Hollinger, Editors. 1995, CRC Press: Boca Raton. p. 293-316.

9. Stedman's Medical Dictionary, 28th Revised Ed. 2006, Baltimore: Lippincott, Williams and Wilkins.

10. Cummings, R.D. and McEver, R.P., C-type lectins, in Essentials in Glycobiology, 2nd ed., A. Varki, et al., Editors. 2009, Cold Spring Harbor Laboratory Press.

11. The American Heritage Dictionary of the English Language, 4th Ed. 2000, Boston: Houghton Mifflin.

12. Lubberts, E., Joosten, L.A.B., Chabaud, M., van den Bersselaar, L., Oppers, B., Coenen-de Roo, C.J.J., Richards, C.D., Miossec, P., and van den Berg, W.B., J. Clin. Invest., 105: 1697-1710 (2000).

13. Rock, K.L. and Shen, L., Immunol. Rev., 207: 166-183 (2005).

14. Goldsby, R.A., Kindt, T.J., Kuby, J., and Osborne, B.A., Immunology, 5th Ed. 2003, New York: W.H. Freeman.

15. Parker, S.P., ed. McGraw-Hill Dictionary of Scientific and Technical Terms, 6th Ed. 2002, McGraw-Hill: New York.

16. Paul, W.E., Fundamental Immunology, 6th Ed. 2008, Philadelphia: Lippincott Williams & Wilkins, Wolters Kluwer.

17. Lackie, J., A Dictionary of Biomedicine, 2010, Oxford University Press.

18. National Research Council, Committee on Biologica Markers, Subcommittee on Immunotoxicology, Biological Markers in Immunotoxicology. 1992, Washington, D.C.: National Academy Press.

19. Kumar, V., Abbas, A.K., and Fausto, N., Robbins and Cotran: Pathologic Basis of Disease, 7th Ed. 2005, Philadelphia: Elsevier Saunders.

20. King, R.C., Stansfield, W.D., and Mulligan, P.K., A Dictionary of Genetics. 2007, Oxford University Press.

21. IPCS, Immunotoxicity associated with exposure to chemicals, principles and methods for assessment. Environmental Health Criteria. Vol. 180. 1996, Geneva: World Health Organization.

22. Yanai, H., Ba, T., Choi, M.K., Kawamura, T., Negishi, H., Nakasato, M., Lu, Y., Hangai, S., Koshiba, R., Savitsky, D., Ronfani, L., Akira, S., Bianchi, M.E., Honda, K., Tamura, T., Kodama, T., and Taniguchi, T., HMGB proteins function as universal sentinels for nucleic-acid-mediated innate immune responses Nature, 462: 99-103 (2009).

23. Sjolander, A., Cox, J.C., and Barr, I.G., ISCOMs: an adjuvant with multiple functions. J. Leukocyte Biol., 64: 713-723 (1998).

24. Waldmann, H., Adams, E., Fairchild, P., and Cobbold, S., Infectious tolerance and the long-term acceptance of transplanted tissue. Immunol. Rev., 212: 301-313 (2006).

25. Martinon, F., Burns, K., and Tschopp, J., The inflammasome: a molecular platform triggering activation of inflammatory caspases and processing of proIL-1β. Mol. Cell, 10: 417-426 (2002).

26. Cammack, R., Atwood, T., Campbell, P., H., P., Smith, A., Vella, F., and Stirling, J., eds. The Oxford Dictionary of Biochemistry and Molecular Biology. 2008, Oxford University Press.

27. Rosenstiel, P., Till, A., and Schreiber, S., NOD-like receptors and human diseases. Microbes Infect., 9: 648-657 (2007).

28. Martin, E. and Hine, R., A Dictionary of Biology. 2008, Oxford University Press.

29. Melchers, F., Karasuyama, H., Haasner, D., Bauer, S., Kudo, A., Sakaguchi, N., Jameson, B., and Rolink, A., The surrogate light chain in B-cell development. Immunol. Today, 14 (1993).

30. Shomer, N.H., Fox, J.G., Juedes, A.E., and Ruddle, N.H., Infect. Immun., 71: 3572-3577 (2003).

ANNEX I – Abbreviations

AAE – Acquired angioedema

ACA – Anticentromere antibody

ADA – Adenosine deaminase

ADAM family protein – A disintegrin and metalloproteinase domain family protein

ADCC – Antibody-dependent cellular cytotoxicity

AFP – α-Fetoprotein

AID – Activation-induced cytidine deaminase

AIDS – Acquired immunodeficiency syndrome

AIH – Autoimmune hepatitis

AIRE – Autoimmune regulator

ALL – Acute lymphoblastic (lymphocytic) leukemia

AMA – Antimitochondrial antibody

AML – Acute myelogenous leukemia

ANA – Anti-nuclear antibody

ANCA – Antineutrophil cytoplasmic autoantibody

ANF – Antinuclear factor

APC – Antigen-presenting cell

APECED syndrome – Autoimmune polyendocrinopathy–candidiasis– ectodermal–dystrophy

APR – Acute-phase response

APS – Antiphospholipid syndrome

ARDS – Acute (or Adult) respiratory distress syndrome

ASA test – Active systemic anaphylaxis test

AT – Ataxia telangiectasia

ATM – Ataxia telangiectasia-mutated

AZT – Azidothymidine

BALT – Bronchus-associated lymphoid tissue

BCG - Bacille Calmette–Guérin

BCR – B-cell receptor

BLIMP-1 – B-lymphocyte-induced maturation protein 1

BLNK – B-cell linker protein

BSF – B-cell stimulatory factor

CALT – Conjunctiva-associated lymphoid tissue

CD – i) Cluster of differentiation, ii) Cluster determinant

CD40L – CD40 ligand

CDR – Complementarity determining region

CEA – Carcinoembryonic antigen

CGD – Chronic granulomatous disease

CLA – Cutaneous lymphocyte antigen

CLL – Chronic lymphocytic leukemia

CMA – Chaperone-mediated autophagy

CMI – Cell-mediated immunity

CML – Chronic myelogenous leukemia

CMV – Cytomegalovirus

ConA – Concanavalin A

CRA – Cytokine release assay

cRBC – chicken red blood cell

CREST – Calcinosis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasias

CRP – C-reactive protein

CSF – Colony stimulating factors

CTL – Cytotoxic T lymphocyte

CTLA-4 – cytotoxic T-lymphocyte antigen-4

DAF – Decay-accelerating factor

DAT – Direct antiglobulin test

DDT – Dichlorodiphenyltrichloroethane

DTH assay – Delayed-type hypersensitivity assay

EAE – Experimental allergic encephalomyelitis

EBV – Epstein–Barr virus

ECF-A – Eosinophil chemotactic factor of anaphylaxis

EGF – Epidermal growth factor

ELISA – Enzyme-linked immunosorbent assay

ELISPOT assay – Enzyme-linked immunospot assay

Erk – Extracellular regulated kinase

ESL – Embryonic stem cell

FACS – Fluorescence-assisted (or activated) cell sorting

FCAS – Familial cold autoinflammatory syndrome

FHL – Familial hemophagocytic lymphohistiocytosis

FITC – Fluorescein isothiocyanate

fMLP – Formyl-methionyl-leucyl-phenylalanine

GABAergic neurons – γ-Aminobutyric acid-responsive neurons

GAD – Glutamic acid decarboxylase

GALT – Gut-associated lymphoid tissue

GBS – Guillain-Barré syndrome

G-CSF – Granulocyte colony-stimulating factor

GM-CSF – Granulocyte–macrophage colony-stimulating factor

GPMT – Guinea pig maximization test

GVH – Graft-versus-host

GVHD – Graft-versus-host disease

HAART – Highly active antiretroviral therapy

HAE – Hereditary angioedema

HEV – High endothelial venule

HIGM – Hyper immunoglobulin M syndrome

HIT – Heparin-induced thrombocytopenia

HIV – Human immunodeficiency virus

HLA – Human leukocyte antigen

HMGB protein – High-mobility group box protein

HMI – Humorally-mediated immunity

HPS – Hypersensitivity pneumonitis

Ia – Immune response-associated (antigen *or* protein), *also* I region-associated

IAT – Indirect antiglobulin test

IBD – Inflammatory bowel disease

ICA – Islet cell antibodies

ICAM – Intercellular adhesion molecule

ICE – Interleukin-1β converting enzyme

ICOS – Inducible co-stimulatory protein

ICOSL – Ligand of inducible co-stimulatory protein (LICOS)

IDDM – Insulin-dependent diabetes mellitus

IDO – Indolamine-2,3-dioxygenase

IDR – Idiosyncratic drug reaction

IEL – Intraepithelial lymphocyte

IFN-γ – Interferon gamma

Ig – Immunoglobulin

IL – Interleukin

IPAF – Interleukin-1β converting enzyme (ICE) protease-activating factor

IPEX – Immunodysregulation, polyendocrinopathy, enteropathy, X-linked

ISCOM – Immunostimulating complex

ITAM – Immunoreceptor tyrosine-based activation motif

ITIM – Immunoreceptor tyrosine-based inhibitory motif

ITP – Idiopathic (or immune) thrombocytopenic purpura

IVCCA – In vivo cytokine capture assay

JAK – Janus-family tyrosine kinase

JAM test – “Just another method” test

JNK – c-Jun protein kinase

KAR – Killer activatory receptor

K cell – Killer cell

KIR – Killer inhibitory receptor, Killer cell immunoglobulin-like receptor

KLH – Keyhole limpet hemocyanin

KLR – Killer lectin-like receptor

KS – Kaposi sarcoma

LAK – Lymphokine- (Lymphocyte-) activated killer cells

LALT – Larynx-associated lymphoid tissue

LBA – Lymphocyte blastogenesis assay

LCA – Leukocyte common antigen

LDL – Low density lipoprotein

LEMS – Lambert-Eaton myasthenic syndrome

LFA – Leukocyte functional antigens

LFA-1 – Lymphocyte function-associated antigen-1

LGL – Large granular lymphocyte

LPT – Lymphocyte proliferation test

LICOS – Ligand of inducible co-stimulatory protein

LKM – Liver–kidney microsomal antibody

LLNA – (Murine) local lymph node assay

LPS – Lipopolysaccharide

LRR – Leucine-rich repeat

LT- Lymphotoxin

LTT – Lymphocyte transformation test

M cell – Microfold cell

Mab – Monoclonal antibody

MAC – Membrane attack complex

MAdCAM-1 – Mucosal addressin cell adhesion molecule-1

MALT – Mucosa-associated lymphoid tissue

MAPC – Multipotent adult progenitor cell

MAPK – Mitogen-activated protein kinase

MASP – Mannan-binding lectin serine peptidase, Mannose□binding-protein□associated serine protease

MBL – Mannose-binding lectin

MBP – Mannose-binding protein

MCAD (MCAS) – Mast cell activation disorder (syndrome)

MCS – Multiple chemical sensitivity

MCTD – Mixed connective tissue disease

MEST – Mouse ear-swelling test

MHC – Major histocompatibility complex

MIGET – Mouse IgE test

MLR – Mixed lymphocyte response/reaction

MMR – Macrophage mannose receptor

MPA – Microscopic polyangiitis

MPO – Myeloperoxidase

MPS – Mononuclear phagocytic system

mTOR – Mammalian target of rapamycin

MTX – Methotrexate

NAA – Natural autoantibodies

NACHT domain – (Protein domain derived from several other acromyms not included in this glossary, namely NAIP, CIITA, HET-E, and TP1)

NALP3 – NACHT domain-, leucine-rich repeat-, and PYD-containing protein 3 (same as NLRP3)

NALT – Nasal-associated lymphoid tissue

NFAT –Nuclear factor of activated T cells

NK cell – Natural killer cell

NKT cell – Cell type intermediate between an NK cell and a T lymphocyte

NLR(P) – NOD-like receptor (protein) *or* Nucleotide-binding domain, leucine-rich repeat-containing protein

NLRP3 – NOD-like receptor protein 3 (same as NALP3)

NOD – Nucleotide-binding oligomerization domain-containing protein

NOD mouse – Non-obese diabetic mouse

NRAMP – Natural resistance-associated macrophage protein

NRL allergen – Natural rubber latex allergen

NSAID – Nonsteroidal antiinflammatory drug

PAF – Platelet activating factor

PALS – Periarteriolar lymphoid sheath

PAMP – Pathogen-associated molecular pattern

PBC – Primary biliary cirrhosis

PBL – Peripheral blood leukocyte, *also* peripheral blood lymphocyte

PBMC – Peripheral blood mononuclear cell

PCA test – Passive cutaneous anaphylaxis test

PCB – Polychlorinated biphenyl

PCDD – Polychlorinated dibenzodioxin

PCDF – Polychlorinated dibenzodioxin

PDGF – Platelet-derived growth factor

PF – Platelet factor

PFC – Plaque forming cell

PHA – Phytohemagglutinin

PKC – Protein kinase C

PLC-γ – Phospholipase Cγ

PLNA – Popliteal lymph node assay

PMA – Phorbol myristate acetate (same as TPA)

PPD – Purified protein derivative

PR3 – Proteinase 3

pre-BCR – Pre-B cell receptor

PRR – Pattern recognition receptor

PSC – Primary sclerosing cholangitis

PWM – Pokeweed mitogen

PYD – Pyrin (N-terminal homology) domain

RA – Rheumatoid arthritis

RADS – Reactive airways dysfunction syndrome

RAG – Recombination-activating gene

RANTES – Regulated upon activation normal T cell expressed and secreted

RARF – Ra-reactive factor

RAST – Radioallergosorbent test

RES – Reticuloendothelial system

RIA – Radioimmunoassay

ROI – Reactive oxygen intermediates

ROS – Reactive oxygen species

RSS – Recombination signal sequence

RSV – Respiratory syncytial virus

SALT – Skin-associated lymphoid tissue

SAPK – Stress-activated protein kinase

SAT – Spontaneous autoimmune thyroiditis

SCA – Single-chain antibody

SCID – Severe combined immunodeficiency

SCLE – Subacute cutaneous lupus erythematosus

SHM – Somatic hypermutation

SIgAD – Selective immunoglobulin A deficiency

SIGLEC – Signaling lectins

SIS – Skin immune system

SLA – Soluble liver antigen

SLE – Systemic lupus erythematosis

SMAC – Supramolecular adhesion complex

SNP – Single-nucleotide polymorphism

SOC protein – Small outer capsid protein

SRBC – Sheep red blood cell

SSc – Systemic sclerosis

STAT – Signal transducer and activator of transcription

TAP – Transporter associated with antigen processing

TCDD – 2,3,7,8-Tetrachlorodibenzodioxin

TCDO – Tetrachlorodecaoxide

TCR – T-cell receptor

TD antigen – Thymus-dependent antigen

TDAR – T-cell dependent antibody response

TdT – Terminal deoxynucleotidyl transferase

TEN – Toxic epidermal necrolysis

TG – Thyroglobulin

TGF-β – Transforming growth factor beta

TIL – Tumor-infiltrating lymphocyte

TLR – Toll-like receptor

TNF – Tumor necrosis factor

TPA – Tetradecanoyl phorbol acetate (same as PMA)

TPO – Thyroid peroxidase

TRA –Tumor rejection antigen

TRAF – TNF receptor-associated factor

TSHR – Thyroid-stimulating hormone receptor

TSTA – Tumor-specific transplantation antigen

tTG – Tissue transglutaminase

TUNEL – TdT-dependent dUTP-biotin nick end labeling

UGT – Uridine diphosphate (UDP)-glucuronosyltransferase

VCAM – Vascular cell adhesion molecule

VLA – Very late activation antigen

WG – Wegener granulomatosis

ZAP-70 – Zeta chain (TCR)-associated protein kinase-70 kDa

ANNEX II – List of chemicals with known effects on the immune system

Major sources used for compiliation of the list were:

IPCS, Immunotoxicity associated with exposure to chemicals, principles and methods for assessment. Environmental Health Criteria. Vol. 180. World Health Organization, Geneva (1996).
IPCS, Principles and Methods/Assessing Allergic Hypersensitization Associated with Exposure to Chemicals. Environmental Health Criteria. Vol. 212. World Health Organization, Geneva (1999).
IPCS, Principles and Methods for Assessing Autoimmunity. Environmental Health Criteria. Vol. 236. World Health Organization, Geneva (2006).
Kaminski, N.E., Faubert Kaplan, B.L., & Holsapple,M.P., Toxic Responses of the Immune System. In: Klaassen,C.D. (ed.) Casarett and Doull´s Toxicology, 7th Ed. McGraw Hill, New York (2008).
Pichler, W.J., ed., Drug Hypersensitivity. Karger, Basel (2007).

A) Pesticides

carbaryl
Insecticide associated with alterations of immunoglobulin levels.

dichlorodiphenyltrichloroethane (DDT)
Insecticide associated with suppression of various types of inconsistent immune responses.

malathion
Insecticide exhibiting both immunosuppressive and enhancing effects.

organotins
Compounds such as the antifouling agent tributyltin, di-n-octyltindichloride and di-n-octyltindichloride that act on maturing and proliferating T-lymphocytes. They are considered prototypes of immunosuppressive chemical agents.

parathion
Insecticide which suppresses the humoral and cell-mediated immune response.

B) Environmental contaminants

hexachlorobenzene
Formerly used pesticide causing increased weight of lymphatic organs and various other immunotoxic effects in rodents.

polychlorinated biphenyls (PCBs)
Chemicals, formerly widely used in technology (e.g., in transformer fluids), congeners of which are immunosuppressive to various degrees, reducing thymus weight and antibody-formation in experimental animals.

polychlorinated dibenzofurans (PCDFs)
Environmental agents whose immunotoxic profile is similar to that of polychlorinated dibenzodioxins.
See also polychlorinated biphenyls.

polychlorinated dibenzodioxins (PCDDs)
Products of incomplete incineration and contaminants in 2,4,5-T (formerly widely used as a herbicide and notoriuously as Agent Orange in the Vietnam War), 2,3,7,8-tetrachlorodibenzodioxin (TCDD) is the most toxic representative of this group of chemicals. It causes *thymic* atrophy and suppression of cell mediated immunity in rodents.
See also *chloracne* in alphabetical entries.

polycyclic aromatic hydrocarbons
Chemicals released during combustion of fossil fuels, including benzopyrene, 7,12-dimethylbenzanthracene, and 3-methylcholanthrene that suppress humoral and cellular immunity.

C) Industrial chemicals

acid anhydrides
Group of reactive chemicals that tend to induce hypersensitivity reactions, such as dermatitis.

benzene
Organic solvent that is toxic to the bone marrow and suppresses lymphocytes.

bisphenol A
Plasticizer with possibly effects on the immune system via an estrogen-receptor-dependent mechanism.

formaldehyde
Highly reactive substance which is an allergen in humans and can potentiate the allergenic effect of other substances.

polyisocyanates
Group of reactive chemicals used in paints, which may induce asthma-like symptoms in isocyanate workers, probably by forming neoantigens.

silica
Inhaled dust particles of silica are toxic to lung macrophages and may depress immune parameters.

vinyl chloride
Monomer for polyvinyl chloride (PVC) production, which may cause a scleroderma-like syndrome.

D) Drugs

D1) with adverse effects

ampicillin
Antibiotic, often accompanied by exanthema, which is potentiated by cytomegalus virus or mononucleosis infection.

carbamazepine
Antiepileptic drug that may cause delayed-type hypersensitivity, leading to a variety of hypersensitivity reactions including life-threatening skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis).

halothane
Inhalational anesthetic that may cause autoimmune and allergic hepatitis due to formation of neoantigen.

hydralazine
Hypotensive drug that may cause autoimmunity, manifested as systemic lupus erythematosus-like syndrome.

α-methyldopa
Hypotensive drug that may induce autoimmune reactions including hemolytic anemia and autoimmune hepatitis.

paclitaxel
Anticancer drug extracted from the Pacific yew tree, which influences microtubule dynamics, causing bone marrow suppression and thrombocytopenia.

penicillamine
Therapeutic chelating agent used to eliminate toxic metals such as in treatment of copper overload, but may also cause autoimmune disease such as myositis.

phenytoin
Antiepileptic drug that can cause a range of hypersensitivity reactions, similar to those caused by carbamazepine. If a patient has a hypersensitivity reaction to one they are likely to have a similar reaction to the other.

procainamide
Antiarrhythmic drug that induces autoimmune disease, manifested as systemic lupus erythematosus-like syndrome.

propylthiouracil
Drug used to treat hyperthyroidism that may induce hypersensitivity reactions, leading to agranulocytosis, hepatitis, or a lupus-like syndrome.

sulfamethoxazole
Antibiotic that may cause hypersensitivity reactions.

D2) immunomodulating

ascomycin, immunomycin, FK 520
Ethyl analogue of tacrolimus that inhibits degranulation of mast cells, acting mainly in the skin. See also tacrolimus.

antihistamine, histamine-1 receptor antagonist
Drug that blocks a histamine receptor on cell surfaces, thereby counteracting the signal-transducing effects of histamine. In immunotherapy, antihistamine drugs are used to suppress the effects of immunoglobulin E (IgE)-induced histamine release from mast cells in various forms of allergy and inflammation.

azathioprine
6-[(1-methyl-4-nitro-1H-imidazol-5-yl)sulfanyl]-7H-purine
Immunosuppressant prodrug that is metabolized to an active species (mercaptopurine), used in organ transplantation and autoimmune diseases.

azidothymidine (AZT), ziduvurine
Thymidine analogue, which inhibits the reverse transcriptase of human immunodeficiency virus and increases the number of circulating CD4+ cells in patients.

cyclophosphamide
Alkylating agent with immunosuppressive features, used to treat some autoimmune diseases.

cyclosporin A
T-cell-specific immunosuppressive drug that binds to cyclophillin, inhibiting the production of IL-2. Used to prevent graft rejection and in the treatment of some autoimmune diseases.

dexamethasone
Corticosteroid that relieves inflammation (swelling, heat, redness, and pain) and is used to treat certain forms of arthritis; skin, blood, kidney, eye, thyroid, and intestinal disorders (e.g., colitis); severe allergies; and asthma. Dexamethasone is also used to treat certain types of cancer.

filgrastim
Analogue of granulocyte colony-stimulating factor (G-CSF) pharmacologically used to stimulate the proliferation and differentiation of granulocytes.

fingolimod, FTY720
Sphingosine-1-phosphate analog, derived from the fungal product myriocin that inhibits migration of lymphocytes and dendritic cells.

FK-506
See tacrolimus.

immunocyanin
Immune stimulating drug derived from *keyhole limpet hemocyanin (KLH)*.

Immunokine™
Commercial preparation of diluted tetrachlorodecaoxide (TCDO).
See tetrachlorodecaoxide (TCDO).

keyhole limpet hemocyanin (KLH)

Large (8-32 megaDalton) multisubunit oxygen-transporting mollusc protein, used to stimulate immune response (cellular and humoral). Also used as a carrier protein for haptens and in immunotherapy of bladder cancer. Smaller subunits are also used (e.g., immunocyanin).

methoxsalen
xanthotoxin
Herbal furanocumarin with photosensitizing properties leading to dermatitis after skin contact. Also used for photochemotherapy of psoriasis.

methotrexate (MTX)
Antimetabolite and antifolate drug used in treatment of cancer and autoimmune diseases.

mycophenolate
Immunosuppressant drug used to prevent rejection in organ transplantation and in treatment of autoimmune disease.

nonsteroidal antiinflammatory drugs (NSAIDs)
Synthetic pharmaceuticals commonly used to treat inflammation and pain of musculoskeletal disorders. These drugs act by inhibiting cyclooxygenase, a key enzyme in prostaglandin synthesis. Common NSAIDs are acetylsalicylic acid (aspirin), indomethacin, diclofenac, and ibuprofen.
NSAIDs may have immunologically relevant adverse effects such as bone marrow depression, aspirin-induced asthma or "salicylate intolerance", a pseudoallergic reaction.

pimecrolimus
Drug structurally related to tacrolimus (fujimycin), which inhibits T-cell activation. It is used for treatment of atopic dermatitis and psoriasis.

prednisone
1,4-pregnadiene-17,21-diol-3,11,20-trione
Synthetic steroid with glucocorticoid action that is used as an antiallergy and immunosuppressive drug and as an anti-inflammatory agent in the treatment of rheumatoid arthritis (RA).

sirolimus
See rapamycin.

rapamycin
sirolimus
Immunosuppressive drug commonly used after organ transplantation to decrease the risk of rejection.

tacrolimus
FK-506
fujimycin
Immunosuppressive drug commonly used after allogenic organ transplantation to decrease the risk of rejection. It inactivates T lymphocytes by inhibiting signal transduction from the T-cell receptor. Although its target (FK-506 binding protein) is different than that of cyclosporin, it inhibits the same pathway and has similar effects on the immune system.

tetrachlorodecaoxide (TCDO)

Chlorite-containing drug used for the dressing of wounds, immunomodulation, and as a protective agent against radiation. It forms a complex with hemoglobin and stimulates macrophages.

vitamin D3
Physiological form of vitamin D that suppresses Th1 cytokines and increases Th2 cytokines.

voclosporin
Immunosuppressive drug that acts as a calcineurin inhibitor.

E) Metals and metalloids

arsenic
Semimetal that is either immunostimulating or immunosuppressing, depending on the chemical species and condition.

beryllium
Metal that, depending on its speciation, upon chronic inhalation at the workplace, may induce "chronic beryllium disease", a severe and persistent hypersensitivity reaction of the airways.

cadmium
Metal of both occupational and environmental importance that, depending on its speciation, has immunostimulating and immunosuppressive effects.

chromium
Metal that, depending on its speciation, may induce hypersensitivity reactions (e.g., chromium eczema)

cobalt
Metal that, depending on its speciation, induces allergic contact dermatitis.

lead
Metal that, depending on its speciation, is immunosuppressive and decreases resistence to infections in rodents.

mercury
Mercury chloride induces autoantibodies and autoimmune disease in sensitive rat strains. Mercury compounds are also immunosuppressive. The organomercury compound thimerosal is a classical preservative in vaccines.

nickel
Metal which is a common contact sensitizer in the general population.

platinum
Platinum salts induce hypersensitivity reactions such as contact dermatitis and respiratory symptoms. Cis-platin, a cytostatic compound, inhibits rapidly proliferating B-cells and T-cells.

F) Miscellaneous

aflatoxin B1, mycotoxin
Potent carcinogenic compound produced by fungi, which causes suppression of antibody response, probably related to its metabolic bioactivation.

enzymes, proteolytic
Proteins that, when airborne, have the potential of any protein to cause hypersensitivity reactions (such as conjunctivitis, rhinitis, or asthma), but may cause additional tissue damage due to proteolysis.

mitomycin C
[(4S,6S,7R,8S)-11-amino-7-methoxy-12-methyl-10,13-dioxo-2,5-diazatetracyclo[7.4.0.02,7.04,6]trideca-1(9),11-dien-8-yl]methyl carbamate
One of a family of antibiotics produced by Streptomyces caespitosus and used as an anti-tumor agent. It may cause pancytopenia.

oxidant gases
Ozone and nitrogen oxides, when inhaled, impair functions of alveolar macrophages and augment pulmonary allergic reactions.

sulfite
Food additive that may cause a pseudoallergic reaction (sulfite-intolerance) in sensitive individuals.

ANNEX III – Autoantibodies in autoimmune disease

a) Autoantibodies in organ-specific autoimmune disorders

Target organ/system	Diagnosis	Autoantibody specificity
Endocrine system		
Thyroid	Hashimoto thyroiditis	Thyroperoxidase (microsomal antigen, 107 kDa)
	Primary myxedema (atrophic thyroiditis)	Thyroglobulin (conformation specific)
	Endocrine ophthalmopathia	Thyroglobulin, acetylcholine esterase
	Basedow disease	Extracellular domain of the receptor for thyroid stimulating hormone (TSH)
Pancreas	Diabetes mellitus type 1, Autoimmune polyendocrinopathy	Insulin-producing β-cells of the Langerhans islets Glutamate decarboxylase (GAD 65 and 67) Insulin Protein IA2 (ICA512/40 kDa) and IAβ (Phogrin/37 kDa) Surface of islet cells
Adrenal cortex	Addison disease, Autoimmune polyendocrinopathy type 2	Microsomes of the adrenal cortex: 21-hydroxylase
	Autoimmune polyendocrinopathy type 1	17-α-hydroxylase
Parathyroid gland	Hypoparathyroidism	Cells of the parathyroid, parathormone
Pituitary gland	Insufficiency of pituitary, autoimmune polyendocrinopathy	Corticotropin, prolactin, growth hormone, steroid-hormone-producing cells
Hypothalamus	Diabetes insipidus, polyendocrinopathy	Vasopressin-producing cells

Hematological system		
Erythrocytes	Hemolytic anemia	Rh-system
	Cold agglutination syndrome	Blood group substance I
	Paroxysmal cold hemoglobinuria	Blood group substance P
Thrombocytes	Idiopathic thrombocytopenic purpura (ITP) Autoimmune thrombocytopenia (AITP)	GP IIb/IIIa (125, 95 kDa), Ib/IX (135/25 kDa and 22 kDa) and V (82 kDa)
Granulocytes	Agranulocytosis	Membrane of granulocytes; NA1/NA2 (Fc receptor type III), NB1 (58-64 kDa glycoprotein) Neutrophilic adhesion glycoprotein complex CD11b/CD18 (CR3, Mac-1, αm:β2 integrin) TSH receptor-like antigen
Gastrointestinal tract		
Stomach	Chronic atrophic gastritis, Pernicious anemia	Parietal cells
	Funicular myelosis	Intrinsic factor H^+/K^+ ATPase α- and β-subunit
Gut	Crohn disease	Pancreas secret Colonic epithelial cells (40 kDa protein) Neutrophils (pANCA)
	Ulcerative colitis	Neutrophils (pANCA)
	Sprue/celiac disease	(Gliadin) Endomysium Reticulin Tissue-transglutaminase

Liver	Autoimmune hepatitis	Nuclei (DNA-histone) (ANA) Smooth muscle antigens (actin) (SMA) Soluble liver/liver-pancreas antigen (LP/SLA) UGD tRNA associated protein Liver-kidney microsomes (cytochrome P450IID6) (LKM1) Liver-membrane antigen (LMA; 26 kDa) Asialoglycoprotein receptor protein (AGPRP)
	Primary biliary cirrhosis	Mitochondria: M2 (subunits of the 2-oxoacid dehydrogenase complex: 70, 56, 52, 45, 36 kDa) Nuclei: Nuclear dots (sp100) Nuclear membrane (gp210) Centromeres
	Primary sclerosing cholangitis (PSC)	Neutrophils (pANCA)
Other organs		
Heart	Dilative cardiomyopathy	Sarcolemma, myolemma
		Mitochondria (M7: FAD-part of flavoenzymes) ADP/ATP nucleotide translocator Calcium channels β-Adrenoreceptor
	Cardiac infarction	Phospholipid
	Atherosclerosis	Oxidized 'low density lipoprotein' (LDL)
Kidney	Idiopathic necrotizing glomerulonephritis	Neutrophils (pANCA: myeloperoxidase)
	Collagen disorders	Nuclei (ANA; see collagen disorders)
Kidney/Lung	Goodpasture syndrome	Glomerular basement membrane (α3 chain

		of type IV collagen)
Muscle	Myasthenia gravis	Acetylcholine receptor
	Myositis	Nuclei (ANA; see collagen disorders)
Skin	Pemphigus vulgaris	Desmosomes (desmoglein 3 ; 130 kDa)
	Pemphigus foliaceus	Desmosomes (desmoglein 1: 160 kDa; plakoglobin: 85 kDa))
	Bullous pemphigoid	Hemidesmosomes, BP 230 (BPAG1: intracellular part of hemidesmosomes) and BP 180 (BPAG2: extracellular part), junction of epidermal cells
	Dermatitis herpetiformis	Dermal-epidermal junctions Jejunal mucosa, reticulin
	Epidermiolysis bullosa acquisita	Type VII collagen
	Systemic lupus erythematosus (SLE), Systemic sclerosis (SSc), Dermatomyositis	Nuclei (ANA; see collagen disorders)
Central nervous system	Polyneuropathy	Gangliosides
	Guillain-Barré-syndrome (GBS)	Gm1
	Neuropsychiatric SLE	CNS-tissue, neuronal structures, phospholipids
	Cerebral vasculitis	CNS-tissue, neuronal structures, phospholipids
	Cerebral infarction	Phospholipids
	Rasmussen encephalitis	Glutamate receptor
	Functional somatic syndromes (fibromyalgia, chronic fatigue, etc.)	Neurotransmitter (i.e., serotonin)
	Funicular myelosis	Intrinsic factor
	Encephalomyelitis disseminata	Myelin basic protein
	Schizophrenia	Perinuclear structures of neurons

	Alzheimer disease	Perinuclear structures of microglial cells
	Amyotrophic lateral sclerosis	Ca^{2+}-channel (L-type)
	Paraneoplastic polyneuropathies	Neuronal and nuclear antigens
Eye	Primary uveitis, keratitis	Epithelial cells of the cornea, lens proteins/crystallins, retinal antigens (retinal-S-protein, rhodopsin, opsin, interphotoreceptor-retinoid-binding protein)
Ear	Sensorineural hearing loss, tinnitus	Structures of the inner ear, nuclei, cytoskeletal antigens

b) Autoantibodies in systemic autoimmune disorders

Disorders	**Autoantibody specificity**	**Target antigen**
Collagen disorders		
Systemic lupus erythematosus (SLE)	Nuclei (ANA)	Different nuclear antigens
	dsDNA	Double stranded DNA
	ssDNA	Single stranded DNA
	Sm	Small nuclear ribonucleoprotein particles (snRNP) MW 29, 28, 16, 13 kDa
	SSA/Ro	Ribonucleoprotein-containing uridine-rich nucleic acid [hY(human cytoplasmic)1, hY3, hY4, hY5]; most important proteins: MW 60, 52 kDa
	Lamin B	Nuclear membrane protein, 70 kDa
	M5	Mitochondrial protein
	Heat shock proteins	90 kDa
	CNS-tissue	Target antigens unknown
	Ribosomal P protein	Ribosomal Phosphoproteins P0, P1, P2
	Phospholipids	Cardiolipin, Phosphatidylserine, β2-glycoptotein

	Thrombocytes	
	Erythrocytes	Rh-system, blood group substances
Mixed connective tissue disease (MCTD)	RNP	Ribonucleoprotein complex with U1snRNA (70, 33, 20 kDa)
Primary Sjögren disease	SSA/Ro	See under SLE; 60, 52 kDa, associated with cytoplasmic hYRNA subunits
	SSB/La	Phosphoprotein (48 kDa), associated with different small RNAs
	Rheumatoid factor	IgG Fc-region
Progressive systemic sclerosis (SSc)	Scl 70	Topoisomerase I: 100 kDa protein, 70 kDa after denaturation
	Nucleoli	RNA-polymerase I, PM-Scl (11-16 proteins), sno (small nucleolar) RNP (i.e. fibrillarin), nucleolus organizing region (NOR) 90
	Centromeres	CENP-A, -B, -C
Poly/dermatomyositis	<u>Aminoacetyl-tRNA synthetases</u>	
	Jo-1	Histidyl-tRNA-synthetase (50 kDa)
	PL-7	Threonyl-tRNA-synthetase (80 kDa)
	PL-12	Alanyl-tRNA-synthetase (110 kDa)
	EJ	Glycyl-tRNA-synthetase (75 kDa)
	OJ	Isoleucyl-tRNA-synthetase (150 kDa)
	KJ	Protein in the transcription process
	SRP	Signal recognition particle
	<u>Nuclear antigens</u>	
	PM-Scl	Antigen in the nucleolus, consistent of 11-16 proteins with MW 20-110 kDa)
	Mi-2	Antigen consistent of 6 proteins
	U1-RNP	70, 33, 22 kDa proteins of U1-snRNP
	Ku	DNS-binding proteins, MW 70 and 80-86 kDa

Rheumatoid arthritis	Nuclei	Antigen not known
	Rheumatoid factor	IgG, Fc-part
	CCP	Cyclic citrullinated peptide
	hsp	Heat shock proteins
	RA33 (hnRNP-complex)	Heterogeneous nuclear ribonucleoprotein-complex (30 proteins)
Vasculitis		
Wegener disease (WG)	cANCA	Antineutrophilic cytoplasmic antibodies, cytoplasmic staining (proteinase 3)
Leukocytoclastic vasculitis	cANCA	Antineutrophilic cytoplasmic antibodies, cytoplasmic staining (proteinase 3)
	pANCA	Antineutrophilic cytoplasmic antibodies, perinuclear staining (myeloperoxidase)
Microscopic angiitis	pANCA	Antineutrophilic cytoplasmic antibodies, perinuclear staining (myeloperoxidase)
Churg-Strauss syndrome	cANCA	See above
	pANCA	See above
Antiphospholipid syndrome (APS)	Phospholipids, Lupus anticoagulant	See aboveCardiolipin, phosphatidylserine, β2-glycoprotein and others
Autoimmune angioedema		
Autoimmune angioedema	C1-inhibitor	C1-inhibitor

ANNEX IV – Therapeutic agents (monoclonal antibodies or fusion proteins) for human autoimmune disorders and tumors

a) Agents for autoimmune disorders

Target class	Molecular target	Therapeutic agent	Name	Disease
Adhesion molecules	α4:β1 and α4:β7 integrin	mAb humanised	Natalizumab	Relapsing/remitting multiple sclerosis Rheumatoid arthritis Inflammatory bowel disease
	ICAM-1	mAb	Enlimomab	Rheumatoid arthritis, stroke
	ICAM-1	20 base pair nucleotide chain hybridising with ICAM-1 mRNA and reducing ICAM-1 expression	ISIS-2301 (Alicaforsen)	Inflammatory bowel disease
B-cells	CD20-specific	mAb, chimeric	Rituximab	Rheumatoid arthritis Systemic lupus erythematosus Multiple sclerosis
		mAb humanised	Ocrelizumab	Rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis
		mAb human	Ofatumumab	Rheumatoid arthritis, multiple sclerosis
	CD22	mAb humanized	Epratuzumab	Autoimmune diseases
	B-cell activating factor (BAFF)	mAb human	Belimumab	

	BAFF and APRIL (proliferation induced ligand)	Fusion protein binding to BAFF and APRIL	Atacicept	Systemic lupus erythematosus, Multiple sclerosis
T-cells	CD3	mAb humanised	Visilizumab	Inflammatory bowel disease, Type 1 diabetes mellitus
		mAb murine	Muromonab-CD3	Rejection after transplantation
	CD25 (IL-2 receptor)	mAb humanised	Daclizumab	Ulcerative colitis
		mAb Chimeric	Basiliximab	Ulcerative colitis
	CTLA4	Immunoglobulin fusion protein	Abatacept	Psoriasis, Rheumatoid arthritis, Multiple sclerosis
	CD58 (LFA-3)	Immunoglobulin fusion protein	Alefacept	Psoriasis
	CD52	mAb humanised	Alemtuzumab (Campath-1H)	Multiple sclerosis
Cytokines	TNFα	mAb chimeric	Infliximab	Rheumatoid arthritisinflammatory bowel disease, psoriasis-arthritis
		mAb human	Adalimumab	Rheumatoid arthritis, psoriasis, Crohn's disease, Spondylitis ankylosans
		Recombinant TNFa-receptor	Etanercept	Rheumatoid arthritis
		mAb human	Golimumab	Rheumatoid arthritis, psoriasis, Spondylitis ankylosans
		Humanized ab to TNFa-fragment	Certolizumab (CPB870)	Rheumatoid arthritis, Crohn's disease
	IL-1	Receptor antagonist	Anankira	Rheumatoid arthritis
	IL-6 receptor	mAb humanized	Tocilizumab	Rheumatoid arthritis

	mAb against IL-6 receptor	Atlizumab	Crohn's disease
IL-15	mAb human	HuMax	Rheumatoid arthritis
IL-12	mAb human	ABT-874/J695	Crohn's disease
IL-12/23	mAb human	Ustekinumab	psoriasis
IL-5	mAb humanised	Mepolizumab	Churg-Strauss-Syndrome, Hypereosinophilic syndrome
TNFα, IL-2, IL-12, IFNγ	decapeptide	RDP58	Ulcerative colitis

b) Agents for tumors

Target class	Molecular target	Therapeutic agent	Name	Disease
Growth factor	VEGF	mAb humanized	Bevacizumab	Colorectal carcinoma, bronchial carcinoma, Breast cancer Macular degeneration
	EGFR	mAb chimeric ab	Cetixumab	Colorectal cancer, head and neck tumors
		mAb human	Panitumumab (ABX-EGF)	Colorectal cancer
		mAb human	Panitumumab	Colorectal cancer
B-cells	CD20	mAb chimeric	Rituximab	Non-hodgkin B-cell lymphoma
		mAb, murine, ^{90}Y-labelled	Ibritumomab-Tiuxetan	Non-hodgkin B-cell lymphoma (radioimmunotherapy)
		mAb, murine, ^{131}I-labelled	Tositumomab	Non-hodgkin B-cell lymphoma (radioimmunotherapy)

		mAb humanised	Ocrelizumab	Hematological cancer
		mAb human	Ofatumumab	CLL, Non-Hodgkin lymphoma, B cell lymphoma
	CD22	mAb humanized	Epratuzumab	Non-Hodgkin-Lymphoma, ALL
	CD23	mAb, chimeric	Lumiliximab	CLL
	HLA-DR	mAb humanized	Apolizumab	Solid tumors, ALL, CLL, non-Hodgkin-Lymphoma
	CD80	mAb chimeric	Galiximab	Non-Hodgkin Lymphoma
T-cell	CD4	mAb human	Zanolimumab	T-cell lymphoma
	CD52	mAb humanised	Alemtuzumab (Campath-1H)	CLL, T-cell lymphoma
	CD33	mAb humanised (loaded with Calicheamicin)	Gemtuzumab - Ozogamicin	AML
	CD25	mAb humanised	Alemtuzumab	CLL, T-cell lymphoma, ALL