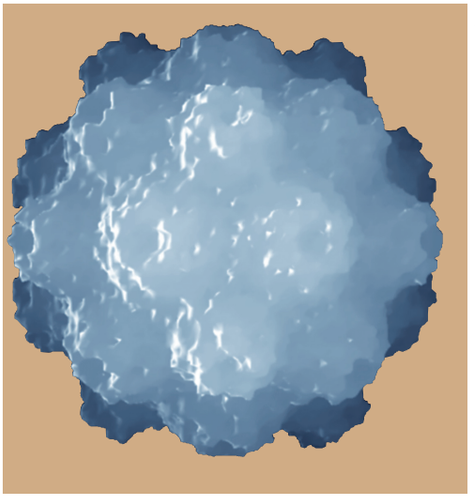


Appendix – Resource Center

A number of sources are available for more detailed investigation of the topics introduced in this text. The level of coverage varies from basic (like this book) to highly advanced investigations of detailed experimental questions found in primary journal articles. The following should provide a useful set of sources for beginning follow-up investigations.

Books of historical and basic value

Although early texts are generally so out of date as to be unusable, three basic "landmark" texts still provide useful information and an appealing richness of coverage:

- Stent GS. Molecular biology of bacterial viruses. San Francisco: WH Freeman, 1963.
- Luria SE, Darnell JE. General virology, 2nd ed. New York: John Wiley, 1967.
- Fenner F, McAuslan B, Mims C, Sambrook J, White DO. The biology of animal viruses, 2nd ed. New York: Academic Press, 1974.

The first of these books is a classic. Not only does it provide basic technical information that is invaluable; it also provides a wonderful description of the origins of molecular biology in the study of bacterial viruses. The author, Gunther Stent, along with J Cairns and JD Watson subsequently edited a collection of reminiscences by many of the original contributors to what we now know as molecular biology and molecular genetics. It was originally published in 1966, and then republished in an expanded version in 1992:

- Cairns J, Stent GS, Watson JD, eds. Phage and the origins of molecular biology. Cold Spring Harbor, NY: Cold Spring Harbor Press, 1992.

In our opinion, for beginners, this more complete historical source does not significantly improve on the simpler descriptions in the first book.

The second text is also full of historical interest. It was written at a time when the field was just beginning to "explode" from the infusion of what is now modern molecular biology. Its style and organization are a model for almost all subsequent texts.

The third book is still more than a little useful for reading about the interaction between viruses and human populations as well as pathogenesis. The overall style and level of coverage provide another milestone in development of the field. Portions covering pathogenesis and immunology were updated in the following text:

- Mims CA, White DO. Viral pathogenesis and immunology. Boston: Blackwell Science, 1984.

Books on virology

- Watson JD, Hopkins NH, Roberts JW, Steitz JA, Weiner AM. The molecular biology of the gene, 5th ed. Menlo Park: Benjamin/Cummings, 2003.

This comprehensive text describes most aspects of modern molecular biology at a level appropriate for advanced undergraduates. There are some excellent sections on gene regulation, and some important bacterial and animal viruses are well covered.

The most comprehensive modern text devoted to virology that contains a wealth of detail concerning individual viruses infecting humans, as well as some detail on the general principles of virology, is the extensive compendium originally conceived by the late Bernard Fields. The set is now in it's fifth edition and is called *Field's Virology*:

• Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA, Roizman B, Straus SE, eds. Field's virology, 5th ed. New York: Lippincott, Williams, and Wilkins, 2006.

The chapters in this book are essentially reviews written by various experts in the field, and as such, the book (of necessity) suffers a bit from unevenness in style and depth of coverage. It is intended for medical and professional students as well as working scientists and is currently being revised for a sixth edition. The third edition of the book was extracted to make it more manageable in size and cost as a medical text and published as:

• Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA, Roizman B, Straus SE, eds. Fundamental virology, 4th ed. New York: Raven Press, 2001.

A slightly less detailed but very useful general coverage of viruses in toto is:

• Granoff A, Webster RG, eds. Encyclopedia of virology, 2nd ed. New York: Academic Press, 1999.

The organization is by subject matter, and its effective use requires some basic background knowledge (like that offered in this book).

Short definitions of terms used in virology can often be found in:

• Mahy BWJ. A dictionary of virology, 3rd ed. New York, Academic Press, 2001.

Detailed aspects of the pathogenesis of virus infections, again organized as a group of specific reviews by individual experts, are covered in:

• Nathanson N, ed. Viral pathogenesis. Philadelphia: Lippincott-Raven, 1997.

This book is difficult and complex, but there are a number of very interesting illustrations that are of value even if one doesn't want to go into the fullest detail concerning any given virus.

Recently a book on viral diseases of humans has been published:

• Strauss E, Strauss J. Viruses and human diseases. San Diego: Academic Press, 2002.

Another useful reference is a medical source:

• Gorbach SL, Bartlett JG, Blacklow NR, eds. Infectious diseases, 3rd ed. Philadelphia: WB Saunders, 2004.

This encyclopedia is very detailed and intended for medical students and physicians. Nevertheless, it contains a lot of basic information concerning the symptoms and course of viral diseases, and is worth a look when a specific subject is of interest.

A myriad of general texts on aspects of virology are available. Perhaps the best recent book that has coverage slightly broader than this one is:

• Voyles BA. The biology of viruses, 2nd ed. St. Louis: Mosby, 2001.

Other books of a relatively equivalent level include:

• Cann AJ. Principles of molecular virology, 4th ed. San Diego: Academic Press, 2005.

• Dimmock NJ, Primrose SB. Introduction to modern virology, 5th ed. Cambridge, MA: Blackwell Science, 2005.

• Levy JA, Fraenkel-Conrat H, Owens, RA. Virology, 3rd ed. Englewood Cliffs, NJ: Prentice Hall, 1994.

Finally, a recent text at a slightly more advanced level is:

• Flint SJ, Enquist LW, Krug RM, Racaniello VR, Skalka AM. Principles of Virology: molecular biology, pathogenesis, and control, 2nd ed. Washington, DC, ASM Press, 2003.

Molecular biology and biochemistry texts

Virology is intimately linked with molecular biology and biochemistry. A number of excellent and detailed texts covering these topics are currently available. Many, like the Watson text mentioned above, have some coverage of viruses. A (partial) listing of some of the best would include the following:

• Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular biology of the cell, 4th ed. New York: Garland, 2002.

The first edition of this book set the standard for comprehensive, molecular biology-based texts that span microorganisms to humans. It is still a fine source.

Others include:

• Berk A, Darnell J, Lodish H, Matsudaira P, Zipursky L, Kaiser CA, Krieger M, Scott MP. Molecular cell biology, 5th ed. New York: Scientific American, 2003.
• Lewin B. Genes VIII. New York: Oxford Press, 2004.
• Mathews CK, Van Holde KE, Ahern KE. Biochemistry, 3rd ed. Menlo Park: Benjamin/Cummings, 1999.
• Stryer L, Berg JM, Tymoczko JL. Biochemistry, 5th ed. New York: Freeman, 2002.
• Voet D, Voet JG. Biochemistry, 3rd ed. New York: Wiley, 2005.

Detailed sources

Many other serials, periodicals, and occasional reviews are available in any good university or medical school library. The primary journals contain detailed, complex, and often opaquely written descriptions of specific experimental studies on one or another aspect of a virus or virus–host interaction. These articles require a lot of background before they make much sense (even to an expert), but often have valuable figures, schematics, and other *bons mots* that could be of use to a beginning student. A typical source might be something like:

• Devi-Rao GB, Aguilar JS, Rice MK, Bloom DC, Garza HH, Hill JM, Wagner EK. HSV genome replication and transcription during induced reactivation in the rabbit eye. Journal of Virology 1997;71:7039–7047.

Major virology journals include *Journal of Virology*, published bimonthly by the American Society of Microbiology (ASM); the bimonthly journal *Virology*, published by Academic Press, and the *Journal of General Virology*, published by (England's) Society for Microbiology. The ASM also publishes journals entitled *Molecular and Cell Biology*, *Journal of Bacteriology, Clinical Microbiology Reviews*, as well as many others that cover detailed subject matter. Secondary journals containing material of less general interest include *Virus Research*, *Virus Genes*, and *Intervirology*. These may not be available in all university libraries.

While the above journals are probably too detailed to be of much interest to the beginning student, a monthly periodical published by the Centers for Disease Control (CDC), *Emerging Infectious Diseases*, provides up-to-date articles on emerging and re-emerging viral infections such as SARS and avian influenza. Though not strictly limited to viruses, these articles are of general interest and are written at a level of complexity about equivalent to *Field's Virology*.

There are also numerous articles concerning viruses and aspects of virology written at a reasonable level of detail that appear periodically in general interest science magazines. The most widely read one is *Scientific American*.

Sources for experimental protocols

Individual laboratories have long had "recipe books" in which basic procedures and reagents are outlined. The applicability of molecular biology and DNA-cloning techniques is so varied

and so general to biological studies that no one person or laboratory can keep in touch with all the methods. To resolve this problem, T Maniatis at Harvard University compiled a general laboratory manual for such techniques. This rapidly became a world standard. The most current edition is:

• Sambrook J, Russell D, Sambrook J. Molecular cloning – a laboratory manual, 3rd ed. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 2001.

This has not been the final word, however. Since techniques constantly are updated and improved, and new methods are developed, no book stays current for long. This problem has been met by the publication of:

• Ausubel FM, Brent R, Kingston RE, Moore DD, Seidman JG, Smith JA, Struhl K, eds. Current protocols in molecular biology. New York: Wiley, 1994–present.

This manual is published in loose leaf and is updated two to four times per year. Updates include revisions, corrections, and new methods. The current compendium runs to several thousand pages, and covers everything from cloning to the use of computers for information on genes. While the methods are only of interest for specific use, often there are short explanatory passages outlining general approaches that are useful to even beginning students. All active research laboratories should have access to this series.

Other specialized sets of technique-oriented references are available. One further excellent four-volume source of general methods for dealing with cell culture and other techniques oriented toward the cell is

• Celis J, ed. Cell biology: a laboratory handbook, 2nd ed. San Diego: Academic Press, 1998.

A reference that is a bit less detailed is:

• Feshney RI. Culture of animal cells: a manual of basic techniques, 3rd ed. New York: Wiley-Liss, 1994.

Finally, a good medical dictionary can be helpful in clarifying a term, and medical and biological encyclopedias have value. One recent source that provides rather succinct but generally well-organized definitions and descriptions is:

• Kendrew J, ed. The encyclopedia of molecular biology. Cambridge, MA: Blackwell Science, 1994.

The Internet

The Internet and the World Wide Web have proved itself an increasingly useful and important source of basic information]. Although addresses change and the web continues to develop rapidly, any good search engine will pull out topical information on a number of viruses, viral diseases, and therapies. (Of special interest are websites maintained by the Centers for Disease Control and Prevention, the National Institutes of Health, the American Society for Microbiology, and other such organizations.) The following URL's were checked active as of this writing (September 2006).

Virology sites

Some websites that you might want to start with (for the time being, Ed Wagner's research pages and his virology course page at UCI are still active – we leave reference here to them as part of our memorial to Ed, and we hope they will be useful to you for as long as they are functional):

• E Wagner: Research page: http://darwin.bio.uci.edu/~faculty/wagner
• E Wagner: Virology course page: http://eee.uci.edu/98f/07426/

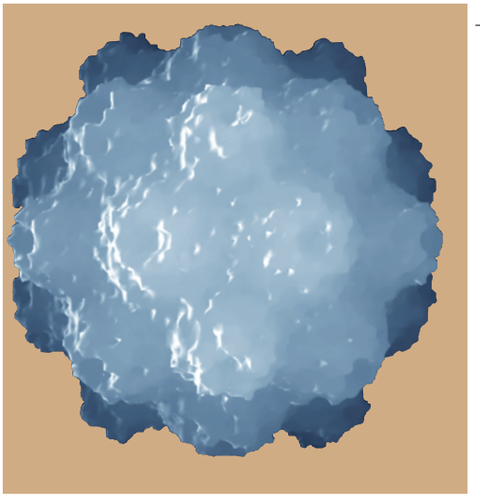
Additional virology web pages are personally organized by various faculty and scientists to ease searches for specific topics in virology. As of summer 2006, the sites listed below seem useful for general background information. Some have self-study questions and sample examinations. It is important to be aware, however, that there is no guarantee that they will survive or be updated regularly.

- The Garry Laboratory at Tulane maintains the most comprehensive website devoted to virology ("All the Virology on the World Wide Web"). The URL is http://www.tulane.edu/~dmsander/garryfavweb.html
- The Viral Bioinformatics Resource Center maintains a useful website (http://athena.bioc.uvic.ca/) that provides access to the sequences of viral genomes and tools for genome analysis. A particularly valuable resource is the site's taxonomic database that allows the student to navigate through the indices of virus families for details about virion structures, summaries of life-cycles, and links to additional resources.
- The University of Wisconsin, Madison, has an Institute of Molecular Virology. Their very useful website is located at http://virology.wisc.edu/IMV/
- The site for the Environmental Protection Agency's microbiology page is: http://www.epa.gov/microbes/index.html
- This site is maintained by the New York State Health Department: http://www.wadsworth.org/databank/viruses.htm
- Michael Rossman's laboratory at Purdue University: http://bilbo.bio.purdue.edu/~viruswww/Rossmann_home/index.shtml
- A PBS site about vaccines and bioterrorism: http://www.pbs.org/wgbh/nova/bioterror/vaccines.html
- An informative website to accompany the book *The Bacteriophages* by Richard Calendar: http://www.thebacteriophages.org/
- A site from the UK devoted to a discussion of virus vectors and gene therapy: http://www-micro.msb.le.ac.uk/3035/peel/peel1.html

Important websites for organizations and facilities of interest

- American Society for Virology (ASV): http://www.asv.org/
- American Society for Microbiology (ASM): http://www.asm.org/
- Melvyl (University of California Library database): http://melvyl.cdlib.org
- Centers for Disease Control and Prevention: http://www.cdc.gov/
- National Library of Medicine: http://www.nlm.nih.gov/
- National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov
- American Association for the Advancement of Science (publisher of the weekly periodical, *Science*): http://aaas.org/

Technical Glossary



abortive infection. Infection of a cell where there is no net increase in the production of infectious virus.

abortive transformation. See **transitory (transient or abortive) transformation**.

acid blob activator. A regulatory protein that acts in *trans* to alter gene expression and whose activity depends on a region of an amino acid sequence containing acidic or phosphorylated residues.

acquired immune deficiency syndrome (AIDS). A disease characterized by loss of cell-mediated and humoral immunity as the result of infection with human immunodeficiency virus (HIV).

acute infection. An infection marked by a sudden onset of detectable symptoms usually followed by complete or apparent recovery.

adaptive immunity (acquired immunity). See **immunity**.

adjuvant. Something added to a drug to increase the effectiveness of that drug. With respect to the immune system, an adjuvant increases the response of the system to a particular antigen.

agnogene. A region of a genome that contains an open reading frame of unknown function; originally used to describe a 67- to 71-amino acid product from the late region of SV40.

AIDS. See **acquired immune deficiency syndrome**.

aliquot. One of a number of replicate samples of known size.

α-TIF. The alpha *trans*-inducing factor protein of HSV; a structural (virion) protein that functions as an acid blob transcriptional activator. Its specificity requires interaction with certain host cellular proteins (such as Oct1) that bind to immediate-early promoter enhancers.

ambisense genome. An RNA genome that contains sequence information in both the positive and negative senses. The S genomic segment of the Arenaviridae and of certain genera of the Bunyaviridae have this characteristic.

amorphous. Without definite shape or form.

aneuploid. A eukaryotic cell with an ill-defined number of fragmented chromosomes, as a result of long periods of continuous passage in culture.

animal model for a (specific) disease. An experimental system using a specific laboratory animal to investigate aspects of pathogenesis of an infectious disease not usually occurring in that animal.

antibodies. Glycoprotein molecules secreted by B lymphocytes with a defined structure consisting of an N-terminal region of variable amino acid sequence (the Fab region), which combines with specific antigenic determinants, and a C-terminal region of constant amino acid sequence (the Fc region), which serves as a biological marker identifying the molecule as part of the immune response.

antigen. Usually a macromolecule that induces an immune response by virtue of small regions that combine with antigen-combining sites on immune cells.

antigen-presenting cell (APC). A cell in which an antigen is processed, followed by expression of epitopes on the surface in conjunction with major histocompatibility antigens. See also **dendritic cells**.

antigen processing. Partial degradation of an antigen within an antigen-presenting cell (APC) followed by its expression at the surface of the APC in the presence of a major histocompatibility protein.

antigenic drift. The slow change in structure of an antigen over time due to accumulated mutational changes in the sequence of the gene encoding the antigen.

antigenic shift. An abrupt change in an antigen associated with a pathogen due to the acquisition of a novel gene substituting for the original one.

antisense oligonucleotide. A short oligonucleotide with a sequence complementary to a specific sequence of nucleotides on a nucleic acid molecule; under investigation as a potential high-specificity target for binding and, thus, inactivating viral genes or mRNA.

antiserum. The plasma fraction containing antibody molecules of the blood of a subject mounting an immune response to the protein or other molecule against which the antibody is directed.

antiviral drug. Any drug that specifically inhibits some process in the replication of a virus without undue toxicity to the host in which the virus is replicating.

antiviral effector molecule (AVEM). One of a number of cellular proteins that function to limit virus replication when activated by the presence of dsRNA in a cell activated by interferon.

antiviral state. A state induced by interferon in a susceptible cell. The cell is partially refractory to virus replication in this state.

apathogenic. Not pathogenic.

APC. See **antigen-presenting cell.**

apical surface. The surface of epithelial cells that face the exterior or an extracellular compartment of the organism. This surface contains specific membrane-associated proteins mediating specific functions; this surface is distinct from the basolateral regions that communicate with adjoining cells.

APOBEC. Apolipoprotein B mRNA editing enzyme complex. This RNA-editing enzymatic activity catalyzes the deamination of specific C residues to U in mRNA.

apoptosis. Programmed cell death; a specific linked set of cellular responses to specific stimuli, such as loss of replication control, that leads to a specific course of changes resulting in cell death.

arboviruses. Arthropod-borne viruses.

archaebacteria (Archaea). One of the two prokaryotic domains of the biosphere. The Archaea are not really bacteria, but the term archaebacteria remains in use.

artificial chromosome. A DNA cloning vector created *in vitro* such that it has the necessary replication structures corresponding to the chromosome of a particular cell. See **bacterial artificial chromosome** (**BAC**) and **yeast artificial chromosome** (**YAC**).

ascites. An accumulation of fluid in the peritoneal cavity of the body.

aseptic meningitis. An infection of the CNS's surface tissue from which no bacteria or metazoan pathogen can be cultured; therefore, by elimination, a viral infection.

assay. A measurement or test.

asymptomatic. Without detectable symptoms.

atomic force microscopy (AFM). A technique for displaying surface features of a sample by recording the deflection of a microscopic probe as it passes over the sample. Resolution with this technique can be on the order of the diameter of a DNA molecule (2.0 nm).

attenuate. Losing virulence due to an accumulation of mutations in virus-encoded proteins mediating pathogenesis during continued passage of a virus in a natural population or in the laboratory.

autoimmune disease. A disease characterized by the subject's immune system attacking and destroying ostensibly normal host tissue.

avian influenze (H5N1). A highly pathogenic type A influenza virus (orthomyxoviruses) with an H5 hemmaglutinin and an N1 neuraminidase. As of this writing, H5N1 is infecting various bird populations around the world, but has not yet mutated to allow direct human-to-human transmission.

AVEM. See **antiviral effector molecule**.

avirulent. A genetic variant of a virulent pathogen that does not cause the disease usually associated with the agent.

B lymphocytes. The immune cells that secrete soluble antibodies.

back mutation. A change in the genome of an organism or virus that returns the genotype to the wild type or original strain.

bacterial artificial chromosomes (BACs). An in vitro constructed cloning vector that utilizes parts of the *E. coli* **F-plasmid** to create a vehicle for inserting foreign DNA into the bacterial chromosome. BACs can be used for the cloning of up to 300 kbp. The cloned DNA is stable, since it becomes part of the bacterial chromosome.

bacterial plasmid. An extrachromosomal circular genetic element with the capacity to replicate as an episome in bacteria. This plasmid often may confer antibiotic resistance on its host. It frequently is utilized for maintaining cloned fragments of DNA.

bacterial restriction. A set of endonuclease-mediated responses to foreign DNA sequences encoded by bacterial genes designed to destroy the genomes of invading bacteriophages and plasmids.

bacteriophage. One of a large group of viruses infecting bacteria.

Baltimore scheme. A scheme of virus classification stressing the mechanism for expression of viral mRNA and the way that information is encoded in the viral genome as primary criteria; formalized by David Baltimore.

base plate. Complex portion of a tailed bacteriophage's capsid that contains projecting protein "pins" mediating the noncovalent interactions between the phage and host cell that lead to injection of the viral genome.

basolateral surface. The "interior" surface of epithelial cells that face other epithelial cells of this and adjoining tissue. The region is distinct from the apical surface that contacts the exterior.

benign tumor. A group of cells forming a discrete mass resulting from limited alterations in cellular growth properties; distinguished from a malignant tumor or cancer in that the cells do not metastasize throughout the body.

bioinformatics. The new field of computational biology that involves the analysis of complex data sets generated by large scale sequencing and **high throughput technology**.

biospheres. The regions of the earth that support life, including all components of that region. Also called the life zone.

bioterrorism. The threat to use or the actual deployment of an infectious agent (fungal, bacterial, or viral) to inflict harm and/or engender fear, especially in a civilian population.

blood–brain barrier. The physical and biochemical parameters creating the relative physical and physiological isolation and physical separation of the CNS from the circulatory system and any pathogens that may be present in it.

bp. Abbreviation for a base pair.

broad host range. Interaction between a virus and host such that can the virus infect a large and diverse number of host organisms. A broad host range for a virus may be associated with the use of a common cellular structure to gain entry.

buoyant density. The density at which a macromolecule or virus "floats" in a gradient under conditions of equilibrium in a centrifugal field.

burst size. Amount of (usually infectious) virus produced from a single infected cell.

cAMP. 3′,5′-cyclic adenosine monophosphate.

cancer. A disease of multicellular organisms characterized by genetic modifications to specific cells that result in the formation of malignant tumors composed of cells without the ability to respond to normal growth-control signals limiting their replication and spread in the body.

cancer cell. A cell isolated from a malignant tumor and displaying the altered growth and other properties associated with the tumor.

cap. The methylated guanosine residue at the 5′ end of eukaryotic mRNA molecules that is added post-transcriptionally as a 5′–5′-phosphodiester.

cap site. The location of initiation of transcription of a specific eukaryotic mRNA.

cap snatching or stealing. The endonucleolytic removal of the 5′-methylated cap region of nascent eukaryotic mRNAs and transfer to a nascent viral mRNA. The process occurs during the replication of orthomyxoviruses and bunyaviruses.

capillary electrophoresis. The separation of charged particles in an applied electric field (10–30 kV) across a capillary tube of small (20–100 mm) diameter. The technique has the advantage over conventional electrophoresis in that it produces quantitatively reproducible separation in a very short (less than one hour) time, using small sample sizes..

capsid. The viral protein shell surrounding the virion core and its nucleic acid genome.

capsomer (capsomere). One of a group of identical protein subunits making up a viral capsid.

carcinogen. A chemical substance that induces a cancer.

catabolite repression. A control mechanism for metabolite use in bacteria mediated by levels of cAMP. It ensures that glucose or other energy sources not requiring expression of inducible metabolic enzymes are utilized first.

caveolae-mediated endocytosis. A process of cellular entry using assemblies of glycosphingolipids and cholesterol in the membrane, along with the protein caveolin. Caveolae-mediated and **lipid raft** endocytosis differ from the classic **clathrin-mediated** entry system involving clathrin-coated pits in that there is no lysosomal fusion step.

CBP1 (cap-binding protein). A eukaryotic ribosome-associated protein involved in the initiation of translation. It functions by binding the 5′-cap structure of eukaryotic mRNA.

CCR5. A cellular chemokine (growth factor) receptor that is used for attachment during HIV infection of macrophage cells.

CD4, CD8. Specific protein antigenic markers found on the surface of different functional classes of T lymphocytes.

cDNA. Complementary DNA; produced by the reverse transcription of an RNA molecule.

cell-mediated immunity (CMI). The portion of the immune response that requires specific recognition between receptors on individual T lymphocytes and antigenic determinants on the surface of antigen-presenting cells.

centrifugation. Subjection of a sample to an artificial gravity field resulting from rapid rotation.

chemokine. An extracellular signaling molecule capable of activating a target cell with appropriate receptors for its recognition.

chicken pox. A childhood disease marked by a distinctive rash and caused by the herpesvirus varicella-zoster virus.

***Chlorella* virus.** A DNA virus of the green algae *Chlorella*.

chorioallantoic membrane. The membrane located between the shell and chicken embryo in an embryonated egg; used as a location for growth of certain viruses such as poxvirus.

cirrhosis. Liver damage characterized by tissue hardening and loss of function and circulation.

***cis*-acting genetic element.** A genetic element that functions only in the contiguous piece of DNA or RNA in which it is present.

CJD. See **Creutzfeldt–Jakob disease**.

clathrin-mediated endocytosis. The process by which ligand molecules are taken into the cell after binding to specific receptors on the cell surface. The ligand–receptor complex then invaginates into an endocytotic vesicle that is surrounded by a clathrin coat. Clathrin is a protein that forms a cage-like structure around the vesicle. Also called receptor-mediated endocytosis.

clinical trial. A formal process for testing the effectiveness of a drug or vaccine on human subjects in a clinical setting.

clonal selection. The selective stimulation of subsets of immune cells reactive with a single antigenic determinant that results in the proliferation of cells specifically responding to that antigen.

clones. Genetically identical biological entities derived from a single parental entity.

cloning. The word has several meanings. First, it means to produce **clones** from a single parent. This might be done in the normal course of replication, such as with bacteria, or by artificial means, such as with nuclear transplant. Second, when the clone organisms (bacterium, for instance) contains a recombinant DNA molecule, it is said that the DNA has been "cloned." In this sense, cloning then refers to the production of cells containing that recombinant DNA.

CMI. See **cell-mediated immunity**.

CNS. Central nervous system.

co-carcinogen. A substance that, when present with a carcinogen, enhances or promotes the development of a tumor.

cold virus. One of a number of RNA genome–containing viruses known to be causative agents of mild infections of the upper respiratory tract and nasopharynx.

complement. A group of serum proteins that bind to an antibody–antigen complex on the surface of a cell, and sequentially undergo a complex maturation process resulting in cell lysis.

complementary strands of nucleic acid. Strands of single-stranded nucleic acid whose sequence is determined by the Watson–Crick base-pairing rules relative to a reference strand.

complementation. The growth of two replication-deficient mutant organisms or viruses that have mutations in different *trans*-acting genes so that each can supply the deficient gene product of the other.

complementing cell line. A cell line that produces those proteins necessary for the growth of defective viruses, especially viruses designed for gene transfer applications.

concatamers. A number of genome-sized DNA regions joined together in a linear array as an intermediate in viral replication, such as during the bacteriophage T4 life cycle.

conditional lethal mutations. Genetic alterations in a specific protein or genetic element that lead to a replication deficiency under controlled laboratory conditions such as high temperature.

confocal microscopy. Technique using a computer-enhanced microscope equipped with laser illumination optics that allow a very small focal plane to be visualized with various wavelengths of light.

conformational epitopes. Antigenic determinants that are only present when the antigen is in a specific (usually native) conformation.

contact inhibition. The cessation of cell replication or movement when the cell is in contact with other cells of the same type.

continuous cell line. A clonal cell line that has been maintained in culture for a large number of passages and is essentially immortal.

copy number. The number of molecules of a particular type (protein, mRNA, gene, plasmid) per cell.

core particles. Poxvirus virions are treated with nonionic detergents to remove the outer wall and membrane and release core particles that can be used to study early transcriptional events.

cosmid. An artificial cloning vector that contains the *cos* sites from bacteriophage λ, allowing the packaging into phage heads of relatively large (up to 45 kbp) DNA inserts.

coupled transcription/translation. The linked process (often in prokaryotic cells) where synthesis of protein encoded by an mRNA molecule commences during ongoing transcription of the mRNA.

CPE. See **cytopathic effect** and **cytopathology**.

C-proteases. Proteolytic enzymes that are involved in the processing of viral precursor proteins. Proteases of this type have a critical cysteine residue as part of their active site.

Creutzfeldt–Jakob disease (CJD). A slow, noninflammatory infection of the human CNS caused by a prion.

cryoelectron microscopy. The preparation of a specimen by embedding it in vitreous (noncrystalline) ice in the absence of stain and its visualization using an electron beam of low intensity. This method preserves much structural integrity of the virion, especially in enveloped viruses.

cryptic ORFs. Open translational reading frames in a eukaryotic mRNA downstream of an efficiently translated one and, thus, one usually not recognized by eukaryotic ribosomes.

CTL. See cytotoxic T lymphocyte.

CXCR4. A cellular chemokine (growth factor) receptor used by HIV for attachment during infection of T cells.

cytochalasin B. One of a number of compounds that interfere with formation of the actin-fiber cytoskeleton that anchors the nucleus inside the cell.

cytokine. One of a group of proteins (usually glycosylated) secreted by cells that have a specific effect on the growth and behavior of target cells. Examples include the interferons.

cytolysis. Cell lysis.

cytopathic effect (CPE). See **cytopathology**.

cytopathology. Observable changes to the appearance, metabolic processes, growth, and other properties of a cell induced by a virus infection.

cytotoxic T lymphocyte (CTL). A sub-type of T lymphocyte (CD8) that has been activated by an antigen and can target and kill a cell that presents that antigen.

defective interfering particles. Defective virus particles that reduce the efficiency of infection by normal virus particles in the same stock.

defective virus particles. Virus particles that are normal or apparently normal in appearance but cannot initiate a productive replication cycle.

defensins. Small (35–40 aa), positively charged, antimicrobial peptides found in both animal and plant cells. Defensins are effective against bacteria, fungi, and enveloped viruses. The function by disrupting the cellular or viral membrane.

denaturation temperature. The temperature at which a biological macromolecule loses its functional higher-order structure by virtue of thermal disruption of hydrogen bonding and other forces contributing to its stability. In the case of double-stranded nucleic acids, this is the temperature where the two complementary strands can no longer associate (also the melting temperature or Tm).

denature. To disrupt the higher-order structure of a protein or nucleic acid–containing macromolecule.

dendritic cells. Cells derived from bone marrow that play a major role in presenting processed antigen to T cells.

deoxyribonucleoprotein complex. A noncovalent complex of protein and DNA that makes up such structures as the eukaryotic chromosome.

dependovirus. A group of parvoviruses whose replication depends upon a concurrent infection of the cell with adenovirus. For example, adeno-associated virus.

desiccation. The act of drying out.

Dicer. A ribonuclease of the RNase III family that cuts long dsRNA into short interfering RNA (siRNA) fragments as part of the RNA interference (RNAi) gene silencing system.

differential display analysis. A method for comparing the population of cellular transcripts in a population of cells before and after an induced metabolic change, such as infection with a virus or stimulation with a cytokine.

differential polyadenylation site usage. The termination of eukaryotic transcription employing alternate polyadenylation signals. The process generates overlapping mRNAs with different 3′ terminal regions.

dilution endpoint. The dilution in a quantal assay at which the agent being tested cannot evoke a positive response.

disease-based classification scheme. One of a number of classification schemes for viruses based on the disease caused.

DNA end problem. A dilemma in the replication of a linear DNA molecule that results from the constraint that the polymerase must synthesize in the 5′ to 3′ direction from a primer. The result is the loss of bases from the end of such a linear molecule, such as occurs in replication of the telomeric regions of eukaryotic DNA.

DNA ligase. One of a class of enzymes involved in DNA replication and repair that join two fragments of DNA together by forming a phosphodiester bond.

DNA polymerase. One of a class of enzymes of complex structure that catalyze the synthesis of a new strand of DNA complementary to the template strand in a primer-dependent reaction.

DNA vaccine. A vaccine comprising a DNA molecule containing the gene for one or more antigenic proteins that can be expressed to elicit immunity when the DNA is injected into a test subject.

dsRNA. Double-stranded RNA.

dsRNA-dependent protein kinase (PKR). The enzyme induced by interferon action on a target cell that phosphorylates eIF-2 in the presence of dsRNA, thus resulting in inhibition of protein synthesis; part of the interferon-induced antiviral state.

EBERs. Two small RNAs transcribed from the early region of Epstein–Barr virus. The presence of these transcripts can be indicative of latent infection. The exact function of these small RNAs is not known.

EBV. See **Epstein–Barr virus**.

eclipse period. The time during the replication cycle of a virus when no infectious virus can be isolated, i.e., between virus adsorption and genome penetration and the appearance of newly synthesized infectious virus.

ED_{50}. Median effective dose; in a quantal assay, the dilution of a pathogen sufficient to ensure that 50% of standard aliquots of that dilution will contain the infectious agent.

effector T cells. Cells of the immune system that act on antigen-bearing cells as part of the immune response. Two major classes include the helper T cells (T_H cells), which interact with antigen-presenting cells in the stimulation of reactive B lymphocytes, and cytotoxic or killer T cells (T_C), which act on antigen-bearing cells to destroy them.

electron microscope. An instrument for viewing biological specimens at a resolution greater than the wavelength of light, using electrons accelerated to a high energy and, thus, short wavelength.

ELISA. See **enzyme-linked immunosorbent assay**.

ELISPOT. A procedure typically used to detect small amounts of cytokines present in tissues or fluids. Similar to an **ELISA**, the primary difference is that the fluid or tissue extract to be tested is placed in a well that has been coated with cytokine-specific antibodies. In an ELISA the antibodies are often added to wells that were previously coated with the tissue or fluid.

encephalitis. An inflammation of the brain or tissues of the upper CNS.

encephalopathy. A noninflammatory disease of the brain.

endocytosis. The process of incorporation of viruses or large molecules into a cell by formation of a specific vesicle at the cell surface that engulfs the material and transports it into the cell's interior.

endonuclease. A nuclease that initiates hydrolysis of a nucleic acid by attack at an interior phosphodiester bond.

endoplasmic reticulum. The complex membrane system in eukaryotic cells that is continuous with the nucleus. It is the site of lipid and membrane synthesis as well as the synthesis of proteins destined to be secreted or remain membrane associated in the cell.

enhancers. *Cis*-acting control sequences in eukaryotic DNA that facilitate transcription from a promoter located a relatively long distance from them.

enteroviruses. A group of RNA viruses replicating in the vertebrate gut and causing mild to severe enteric disease.

env. The gene encoding the polyprotein translation product that contains the envelope glycoproteins of a retrovirus.

envelope (membrane). The lipid bilayer with associated proteins that encompasses a cell or a virus.

enzyme-linked immunosorbent assay (ELISA). An enzymatic method for measuring an immune reaction by binding an enzyme to the Fc region of an antibody molecule and using the activity of this enzyme to indicate the presence of the antibody to which it is bound.

epidemiology. The study of the spread and control of infectious disease in human populations.

epidermis. The outer surface of the skin.

episome. An extrachromosomal (usually circular) genetic element able to replicate in concert with chromosomes of the cell in which it resides.

epitopes. Small regions of (usually) hydrophilic amino acids making up specific antigenic determinants in protein antigens.

epizoology. The study of the spread and control of infectious disease in nonhuman populations.

Epstein–Barr virus (EBV). A human herpesvirus.

Epstein–Barr nuclear antigens (EBNAs). A series of six Epstein–Barr virus proteins produced during latent infection and found within the nucleus. These proteins likely are involved in the establishment and maintenance of latency.

error frequency. The rate of introduction of errors during the replication of a DNA or RNA genome.

etiology. The cause of a disease or pathologic condition.

Eubacteria. One of two prokaryotic domains of the living world, the other being the Archaea.

eukaryote. One of two kinds of cells that constitute living systems. Eukaryotes have internal membrane surrounded structures, especially a membrane defined nucleus containing the genetic material.

eukaryotic translation initiation factors (CBP1, eIF-2, eIF-3, eIF-4A, eIF-4B, eIF-4C, eIF-4F, eIF-5, eIF-6). Ribosome-associated proteins that function in the initiation of translation of an open reading frame on eukaryotic mRNA.

exocytotic (exocytic) vesicles. Membrane vesicles within a cell that carry macromolecules or viruses for release at the cell surface.

exons. The portions of RNA that remain as mature mRNA after the removal of introns by splicing.

exonuclease. A progressive nuclease that attacks its polynucleotide substrate only from a free end.

explant. The removal of intact tissue from an organism followed by maintenance in culture medium.

extremophile. An organism that can grow at extreme limits of environmental conditions, such as high temperature (thermophile) or high salt (halophile).

F pilus. See **sex pilus**.

Fab region. The N-terminal half of an antibody molecule that has both regions of constant and variable sequences. The antigen-combining sites are in the regions of variable sequence.

Fc region. The C-terminal half of an antibody molecule that shares the same sequence as all other antibodies of that class.

feeder layer. A layer of cultured cells included with explanted tissue to provide optimal conditions for survival of the tissue.

feline panleukopenia. A (generally) fatal viral disease of cats, characterized by extreme reduction in circulating leukocytes (white blood cells).

fertility factor (F′ factor). A double-stranded DNA plasmid found in certain bacteria that confers the ability to transfer DNA from one cell to another by conjugation. The F′ factor or plasmid encodes genes that carry out this process, including genes for the F pilus, the bacterial structure that links two cells during transfer.

flu. See **influenza**.

fluor. A substance that absorbs light of a particular wavelength and subsequently emits light, usually of a lower wavelength. The process is called fluorescence.

focus of infection. Identification of areas of cells that have been infected with virus on a tissue culture plate. The areas are recognized by the **cytopathology** produced by the virus in question. Such areas may be observable microscopically or, in some cases, macroscopically. Foci of infection may be used quantitatively for the enumeration of biologically active virus particles.

frame shift. A mutation that affects the sequence of the encoded protein by altering the translational reading frame.

fulminant infection. A severe, sudden, often fatal infection characterized by rapid invasive spread of the infectious agent; often refers to a particularly severe form of hepatitis.

fusion (membrane fusion). The process in which the membrane envelope of a virus combines with a cell membrane or vesicle in the process of virus entry.

***gag*.** The gene encoding the polyprotein translation product that contains the capsid proteins of a retrovirus; the group-specific antigens of a retrovirus.

gene therapy. The treatment of a genetically based disease by the artificial insertion of a corrected version of the gene in question into the patient by one of several mechanisms.

genetic marker. A genetic characteristic that can be screened or selected for.

genetic recombination. The creation of new genotypic arrangements by the breakage and rejoining of chromosomes.

genome. The nucleic acid molecule that encodes the genetic information of an organism.

genomics. The study of the sequence, structure and function of genetic information, especially using computational methods for the analysis of large data sets.

genotype. The genetic makeup of an organism.

German measles (rubella). A usually mild rash and fever caused by an RNA virus, characterized by severe neurological damage to a fetus in the first trimester of gestation.

glycoproteins. Proteins that have sugar residues covalently linked to specific amino acids. Such proteins are often secreted from cells or associated with membranes in such a way that the major portion projects through the membrane.

glycosylation. The process of adding sugar residues onto membrane and excreted glycoproteins in the Golgi apparatus.

Golgi apparatus. Vesicles in the eukaryotic cell that receive newly synthesized lipids and proteins from the endoplasmic reticulum and transport them to the correct location in the cell. Specific chemical modifications to the proteins and lipids transported take place in the Golgi apparatus.

growth factors. Complex macromolecules that function to signal specific cells to replicate.

HAART. Highly active antiretroviral therapy. The use of four or five different antiviral drugs in an attempt to dramatically reduce the viral load of a patient infected with HIV.

hantaviruses Members of the *Bunyaviridae*, the hantaviruses have single-stranded, segmented RNA genomes. Originally named for Hantan virus, the causative agent of Korean hemorrhagic fever, the group now includes viruses that cause adult respiratory distress syndrome (for instance, Sin Nombre virus).

HCCs. See **hepatocellular carcinomas**.

helicase. One of a class of enzymes involved in DNA replication that unwind DNA by catalyzing a local denaturation of the DNA duplex at the point of action.

helix. A spiral.

helper virus. A virus in a mixed infection (usually in cultured cells) that provides a complementing function so that a coinfecting defective virus can replicate.

hemagglutination (hemadsorption). The ability of a virus membrane or a virus-infected cell to stick to red blood cells, caused by the action of one or several specific viral glycoproteins.

hepatitis virus. One of a group of viruses (many unrelated) that target the liver.

hepatocellular carcinomas (HCCs). Malignant tumors derived from cells of the liver.

herd immunity. A qualitative state in a population exposed to an infectious disease where the existence of a sufficient number of recovered and immune individuals restricts the spread of the disease.

herpes simplex virus (HSV). One of two closely related neurotropic human viruses containing a DNA genome and characterized by the ability to form latent infections. HSV type 1 (HSV-1) normally infects facial tissue while HSV-2 infects genital tissue.

herpes zoster virus (HZV). The causative agent of chicken pox.

herpesvirus. One of a large group of related viruses containing large DNA genomes and possessing a similar structure whose infection is characterized by establishment of a latent infection.

hexon. A viral capsid protein subunit that forms a complex with five other similar subunits.

high throughout (HT) technology Methodology that uses miniaturization and computer analysis to examine very large numbers of samples of nucleic acid or protein for their expression and or interactions. Microarrays are one kind of tool used in HT.

HIV. See **human immunodeficiency virus**.

homeostasis. A system that is maintained in equilibrium in a stable physiological state is said to be in homeostasis.

host range. The organism or group of organisms that a virus can infect.

HSV. See **herpes simplex virus.**
HTLV. See **human T-cell leukemia virus.**
human immunodeficiency virus (HIV). A human retrovirus; the causative agent of AIDS.
human T-cell leukemia virus (HTLV). A human retrovirus that is a causative agent of some forms of leukemia.
humoral immunity. Immunity due to antibody molecules circulating in the blood and lymphatic system.
hybrid (nucleic acid hybrid). A double-stranded nucleic acid molecule formed by Watson–Crick base pairing of a given sequence with its complementary sequence, which can be either RNA or DNA.
hybridoma cell. A cell derived by the fusion of an antibody-secreting B cell and a myeloma cell. Hybridomas are clonal and immortal, and secrete the antibody that was secreted by the parental B cell.
hydrophilic. Used to describe a molecule or portion thereof that is hydrated in solution due to energetically favorable interactions with water molecules.
hydrophobic. Used to describe a molecule or portion thereof whose interaction with water molecules is energetically unfavorable.
HZV. See **herpes zoster virus**.
i.c. See **intracranial or intracerebral**.
ICAM. See **intercellular adhesion molecule**.
icosahedron. A regular solid polygon made up of 12 vertices and 20 faces.
ID_{50}. Median infectious dose; in a quantal assay, the dilution at which half the tested aliquots are able to initiate an infection, i.e., contain infectious virus.
IFN. See **interferon**.
immunity. The ability to resist or defend against a pathogen by innate immune responses or acquired immune responses to particular antigens by clonal selection of reactive lymphocytes.
immunofluorescence. A method of detecting and localizing an antibody bound to its cognate antigen by use of a fluorescent dye attached to the Fc region of the antibody molecule. This allows microscopic observation using ultraviolet illumination.
immunologically naïve. Refers to a subject that has never been infected with the infectious agent in question.
IN. The retrovirus gene encoding the enzymatic function that catalyzes the integration of proviral cDNA into the host chromosome.
in situ hybridization. One of a number of methods for localizing a specific nucleic acid sequence or species within a cell, accomplished by fixing the cell, making it permeable, and hybridizing an appropriate probe under conditions where cellular structure is maintained.
inapparent infection. An infection not characterized by overt symptoms of disease, but in which there is active replication of the pathogen.
inbred. Characteristic of offspring between two genetically closely related parents.
incubation period. The time between initial infection and the onset of notable symptoms of a disease.
index case. The first documented case in an epidemiological investigation of a disease outbreak.
inducible genes. Genes whose expression can be induced under appropriate conditions.
influenza (flu). A generally mild infectious disease of the upper respiratory tract caused by a group of viruses with segmented RNA genomes and characterized by rapid genetic change.
informed consent. Permission given for an experimental medical or research procedure only after a full disclosure of the possible dangers to the individual and the benefit to medical knowledge.

initiator tRNA. *N*-formylmethionine-tRNA (fMet tRNA), which initiates the first amino acid in translation of bacterial proteins. In eukaryotic cells, the initiator tRNA is Met-tRNA with no formylation.

innate immunity. Also called nonspecific immunity, this is the collection of structures and responses to an invading pathogen, including anatomical barriers, the complement system, neutrophils, macrophages, and the interferon response.

inoculation. Process of introducing a substance into an organism.

integral membrane protein. A cell membrane-associated protein within but not extending appreciably beyond the membrane envelope cell.

intercellular adhesion molecule (ICAM). One of a large family of glycoproteins projecting through the cellular envelope that mediate the association between cells and between cells and surfaces; used by some viruses (notably poliovirus) as a receptor for entry.

interference. In a mixed virus infection, a phenomenon where some function encoded by the interfering virus reduces the efficiency of replication of the wild-type virus. See **defective interfering particles**.

interferon (IFN). A group of proteins (cytokines) secreted by virus-infected and certain other cells that act to induce a specific set of cellular antiviral and antitumor responses in other cells.

interleukin. A cytokine secreted by an effector cell of the immune system that functions to stimulate other immune cells.

internal ribosome entry site (IRES). A feature in the secondary structure near the 5′ end of a picornaviral RNA genome that allows eukaryotic ribosomes to bind and begin translation without binding to a 5′ capped end.

intracellular trafficking proteins. Intracellular proteins whose main function is to recognize specific molecules and guide them to the appropriate subcellular location.

intracerebral (i.c.). Literally, in the cerebrum. However, commonly used to mean in the brain, such as an injection route.

intracranial (i.c.). General term for injecting virus into the brain of an animal to assess viral replication or virulence.

intravenous (i.v.). Injection of a substance (or virus) into the vein. In the mouse, this typically means injecting into the tail vein.

introns. The portions of a eukaryotic RNA removed by splicing.

iontophoresis. Movement of a positively charged compound in an electric field.

IRES. See **internal ribosomal entry site**.

isoform. One of different structural forms of a protein. Isoforms may differ in their activity.

i.v. See **intravenous**.

Jennerian vaccine. A live-virus vaccine that elicits an immune response to a related pathogenic virus infecting another species.

kb. Abbreviation for kilobases (thousand bases); used in designating the size of DNA and RNA. If the molecules are double stranded, the appropriate unit is kilobase pairs (kbp).

keratinized tissue. Tissue marked by a large amount of keratin, such as at the surface of the skin, the cornea, and hair.

killed-virus vaccine. A vaccine made up of a virus suspension that has been chemically treated so that it is no longer able to cause a productive infection.

knock-out (KO) mouse. A type of transgenic mouse that has been engineered in such a way that a gene is interrupted or deleted such that the function of that gene is altered. KO mice that have deletions in components of immune effectors (such as cytokines) are useful in the study of viral pathogenesis.

Koch's rules. A set of criteria that must be met to demonstrate that a specific microorganism is the causative agent of an infectious disease; named for Robert Koch, the 19th-century German microbiologist who first formulated them.

Kozak sequence. The sequence ANNAUGG, which was identified by Marilyn Kozak as being a favored sequence for the initiation of protein translation on eukaryotic mRNA.

kuru. A human encephalopathy caused by a prion and associated with ritualized funeral cannibalism.

lagging strand. The strand of DNA being replicated in which synthesis is discontinuous.

λ arms. Distal ends of the linear lambda genome, containing information for the replication of the viral DNA. The lambda arms are used as parts of cloning vectors designed to take larger inserted DNA sequences.

Last Universal Common Ancestor (LUCA). In an evolutionary cladogram, the (usually theoretical) common ancestral form or forms that precede the development of further diverging forms. For instance, the ancestral cell or cells that led to the development of both prokaryotes and eukaryotes.

latency-associated transcripts (LATs). Transcripts expressed by many neurotropic herpesviruses during the latent phase of infection.

latent infection. Usually refers to a period following acute herpesvirus infection in which the viral genome is present in specific cells, but in which genes encoding the replication genes are not expressed and viral replication does not take place.

LATs. See **latency-associated transcripts**.

LD_{50}. Median lethal dose; in a quantal assay, the dilution at which half the tested aliquots are able to initiate a lethal infection, i.e., contain sufficient infectious virus to kill the test subject.

lentivirus. A group of retroviruses, such as HIV and visna virus, characterized by a slow, progressive pathogenic course.

leucine zipper. A protein motif that involves the hydrophobic interaction between two amphipathic helices in which one side of each helix contains an alignment of leucine residues.

Leviviridae. A family of positive-sense, single-stranded RNA bacteriophages, including MS2.

linker-scanning mutagenesis. A deletion and replacement strategy in which specific base pairs of a sequence are altered in vitro without affecting the relative spatial arrangements and reading frames.

lipid-raft-mediated endocytosis. Entry into cells mediated by domains of lipids on the outer surface of the membrane, featuring glycosphingolipids and cholesterol. Similar to **caveolae-mediated** entry, but without the presence of the protein calveolin.

live-virus vaccine. A vaccine made up of a virus that has been specifically attenuated, usually by serial passage in a nonhuman host cell.

long terminal repeat (LTR). The 5′ and 3′ terminal regions of the proviral-integrated DNA of a retrovirus that contains control regions for viral RNA transcription.

LTR. See **long terminal repeat**.

lymph nodes. Small bodies of lymphatic tissue within the lymphatic system to which antigenic material is transported by antigen-presenting cells.

lyophilize. Freeze-dry.

lysogeny. Ability of certain bacteriophages (notably, bacteriophage λ) to integrate its genome into that of the host bacteria and remain associated as a genetic passenger as the bacteria replicate.

mAbs. See **monoclonal antibodies**.

macrophage. The primary antigen-presenting cell of the lymphatic system.

macropinocytosis. The entry into the cell of large quantities of fluids from the extracellular space.

major histocompatibility complex The complex of surface glycoproteins, including the major histocompatibility protein, involved in antigen presentation during the immune response. MHC I and MHC II are both involved in this response.

major histocompatibility protein A complex set of membrane glycoproteins encoded by the major histocompatibility complex (MHC). These proteins are on the surface of an antigen-presenting cell and determine whether or not an immune cell recognizes the presenting cell as "self." This is a necessary step in mounting an immune response.

male-specific phage. A bacteriophage that uses the sex pilus of the host cell as a receptor.

malignant tumor. See **cancer**.

MAVS (mitochondrial antiviral signaling) protein. A feature of the **innate immune** response. MAVS mediates the action of NF-κ-B and IRF-3, transcription factors involved in the expression if β-interferon, and therefore a stimulation of the antiviral state in the cell.

MCSs. See **multiple cloning sites**.

meningitis. An infection of the lining of the brain and brain stem.

metastasis. The process by which a cancer (malignant) cell breaks away from the tumor in which it originated, spreads to a new location in the body, and establishes a new tumor.

MHC. See **major histocompatibility complex**.

MHC-I. See **major histocompatibility complex**.

MHC-II. See **major histocompatibility complex**.

microarrays. An ordered series of small (<200 micron) spots of material (nucleic acid or protein) immobilized on a solid surface (see also microchip) such that their interaction with a target molecule in solution can be observed. Microarrays usually contain thousands of such sample spots.

microchip. A small glass surface containing thousands of immobilized samples to be used in a microarray analysis. If the samples are DNA, it may be called a DNA chip or a genome chip.

microglial cells. Cells of the CNS that function as immune cells.

mimivirus. The largest known virus to date. Mimiviruses have ds DNA genomes and a capsid that is 400 nm across. The capsid is decorated with 100-nm filaments, making the overall size of the particle 600 nm, larger than some small cells.

mixed infection. A (viral) infection in which two or more distinct genotypes are able to infect the same cell or individual at the same time.

MOI. See **multiplicity of infection**.

molecular mimicry. The immunological resemblance between two unrelated proteins, for instance, a viral protein and a cellular protein. The resemblance usually involves one part of the protein structure. Such mimicry can lead to immunological consequences for the host during a viral infection, such as precipitation of autoimmune phenomena.

monoclonal antibodies (mAbs). Antibodies produced by a single clone of identical B cells or hybridoma cells.

monopartite genome. A viral genome made up of a single segment.

monospecific. An antibody or antiserum preparation that reacts only with the antigen of interest.

morbidity. A reference to the prevalence, incidence, or severity of a particular disease. Morbidity is distinguished from mortality, which references the death rate from a particular disease.

mosaicism. Refers to organized tissue in which there is more than one distinct genotype intermixed with another.

mucosa. The epithelial layer lining the digestive, respiratory, or urogenital tract.

multipartite genome. A viral genome comprising two or more fragments.

multiple cloning sites (MCSs). Sequences of closely spaced restriction enzyme cleavage sites constructed into a cloning vector to make available several possible points of insertion for DNA.

multiple sclerosis. A neurodegenerative, autoimmune disease of the CNS. There is good evidence that at least some forms result from a complication caused by the persistence of an infectious agent (probably a virus) from an acute infection that occurred many years previously.

multiplicity of infection (MOI). Average ratio of infectious virus particles to target cells in a given infection.

mutation. An inheritable change in the base sequence of the nucleic acid genome of an organism.

Mx. One of a family of proteins induced by interferon action on a target cell. Many of these proteins have unknown functions, but MxA specifically interferes with the initial infection of cells by influenza and vesicular stomatitis virus.

myelitis. Inflammation of the spinal cord.

myeloma cells. Immortal tumor cells derived from lymphocytes. Such cells are useful in creating hybridomas to produce monoclonal antibodies, but they do not produce normal antibodies themselves.

myristoylation. Modification of a protein by the covalent addition of myristic acid to specific glycine residues. Myristoylation gives the protein a hydrophobic (fatty acid) anchor for membrane insertion.

myxoma virus. A poxvirus that normally infects South American hares. It was introduced (with mixed success) into Australia in an attempt to control the devastating increase in the population of European rabbits introduced by English settlers.

narrow host range. Interaction between virus and host such that only very limited kind of host cells are susceptible to infection. HIV has a narrow host range in that it infects only human cells with certain specific cell surface receptors.

necrosis. The unscheduled or unprogrammed death of cells or tissues. Necrosis is in contrast with programmed cell death (see **apoptosis**).

negative-sense RNA. An RNA molecule whose sense is opposite that of mRNA.

negative(–)-sense RNA virus. A single-stranded RNA virus whose genome is the opposite sense of mRNA. The viral genome must be transcribed into mRNA by a virion-associated enzyme as the first step in virus gene expression.

negative strand. See **negative sense**.

neoplasm. A tumor or localized group of proliferating cells that have become independent of the normal control of cell replication.

neuroinvasive. Refers to the specific ability of a virus to gain access to or "invade" the nervous system from the periphery. Ultimately this involves breaching the blood–brain barrier.

neurotropic virus. A virus targeting cells of the nervous system.

neurovirulent. Refers to the ability of a virus to cause death by replication in the nervous system. Often refers to replication specifically within neurons of the CNS.

nonpermissive cell. A cell that will not support the (efficient) replication of a specific virus.

nonpermissive temperature. The temperature at which a conditionally lethal, temperature-sensitive mutant will be nonfunctional.

nonproductive infection. An infection in which the virus interacts with the host cells so that its infectivity is lost, but no progeny virus are produced.

nonstructural protein. In a virus infection, a protein expressed by the virus that does not function or *is not* found in the infectious virus particle. See **structural protein**.

northern blot. Technique for transfer of RNA, separated by agarose gel electrophoresis, from the gel to a membrane, usually nitrocellulose. The RNA can then be analyzed with hybridization probes. The technique is named to distinguish it from the Southern blot, named for its developer, Edward Southern. (see **Southern blot**).

nosocomial. An infection associated with or acquired during a stay in hospital or health care facility such as a nursing home.

nuclear location signal (NLS). A short sequence of amino acids, rich in lysine, at the amino terminus of proteins destined to be transported into the nucleus of the cell.

nucleoprotein. A protein–nucleic acid complex.

Oct1. The cellular octamer-binding protein that binds to eight nucleotides in double-stranded DNA with the nominal sequence TATGARAT (R is any purine). This protein serves as an "adapter" for the binding of the HSV α-TIF transcriptional activator to enhancers of immediate-early promoters.

Okazaki fragments. Short fragments of nascent DNA synthesized using an RNA primer that is an early intermediate of DNA chain growth on the discontinuous (lagging) strand.

oligoA synthetase. 2′,5′-oligoadenylate synthetase (2′,5′-AS): the enzyme that polymerizes ATP into 2′,5′-oligoadenylate; activated by double-stranded RNA and induced by interferon activation of a target cell.

oncogenes (c-onc, v-onc). Genes encoding the proteins originally identified as the transforming agents of oncogenic viruses, some of which were shown to be normal components of cells; v-onc is the viral version of an oncogene while c-onc is the cellular version of the same gene.

open translational reading frame (ORF). A sequence of bases read three at a time between a translational initiator signal (AUG) and a translational termination signal (UAA, UAG, or UGA) in an mRNA or in the DNA encoding that mRNA Each triplet of bases specifies a specific amino acid in the protein encoded by the ORF.

operator. The region of a regulated bacterial gene to which the product of a regulatory gene binds to modulate transcription.

operon. A set of regulated genes in bacteria expressed as a single transcript modulated by the activity of a nearby regulatory gene.

opportunistic infection. An infection that takes advantage of a depleted or deficient immune system to establish itself in a host. AIDS has, as one of its sequelae, opportunistic infections by otherwise innocuous pathogens.

opposite polarity. The orientation of a strand of nucleic acid whose phosphodiester backbone is in the opposite 5′ to 3′ direction relative to another strand.

ORF. See **open translational reading frame**.

ORFeome. The map of all possible translational open reading frames (ORFs) with a genome or set of genomic sequences.

ori. See **origin of replication**.

origin-binding protein. A protein involved in initiating rounds of DNA (or RNA) replication by binding to the specific origin sequence.

origin of replication (ori). Specific site in a DNA or RNA genome at which a round of replication is initiated.

outbred. Results of a genetic cross between two unrelated organisms.

packaging signal. A specific sequence of bases within the genome of a virus that functions in the association and insertion of the genome into the procapsid.

palindromic sequence. A sequence of nucleotides in a double-stranded molecule that is self-complementary and, thus, has the same 5′ to 3′ sequence on both complementary strands; for example, GATATC.

palliative treatment. A treatment of a disease or condition designed to minimize discomfort.

pandemic. An epidemic infection that involves a large percent of the world population during a single period of time.

papillomaviruses. A large group of viruses with DNA genomes that are classified as papovaviruses and cause warts.

parameters (of an experiment). Measurable characteristics of an experiment.

particle to PFU ratio. Ratio of total virus particles to infectious particles in a specific virus stock.

parvovirus. One of a group of viruses with small, single-stranded DNA genomes.

passage (serial passage). In virology, the sequential infection, harvest, and reinfection of a virus into a host or cell culture.

pathogen. A disease-causing organism or entity.

pathogenesis. The mechanism of causing a disease.

PCNA (proliferating cell nuclear antigen). A protein involved in DNA replication in eukaryotic cells. One of a group of cyclins, PCNA is an accessory protein of DNA polymerase delta, and is involved in leading strand elongation during replication.

PCR. See **polymerase chain reaction**.

penton. A subunit protein of virion structure that interacts with four other similar proteins to form a portion of the capsid.

Peyer's patches (gut-associated lymphatic tissue). Lymphatic tissues in the gut that allow antigenic proteins and pathogens to interact directly with the immune system.

phagemids. Cloning vectors constructed with a combination of single-strand DNA phage (e.g., f1) and plasmid genes. Phagemids are able to replicate as single-strand or double-strand molecules.

phenotype. The observable characteristics of an organism that are determined by its genetic makeup.

phylogenetic tree. A diagrammatic illustration of calculated evolutionary relationships between living things (organisms or viruses).

picornavirus. Small viruses with RNA genomes. Poliovirus is an example.

pilot protein. A protein associated with the genome of tailed bacteriophages that functions to begin the process of genome injection into the host cell once the cell wall has been breached through the association with the base plate.

placebo. An inert or innocuous substance used as a negative control for testing a drug in clinical trials.

plaque-forming unit (PFU). A unit of infectious virus determined by the ability of the virus to form a plaque or area of lysed cells on a "lawn" of susceptible cells.

plasmid-like replication. The replication of an extrachromosomal DNA element, especially a circular molecule such as the genome of SV40 or polyomavirus.

plasmodesmata. The cytoplasmic connections between plant cells.

Poisson analysis. The statistical analysis of the probability of a given event happening after a small number of trials.

polarity. For a nucleic acid, the direction in which the sequence is read, i.e., 5′ to 3′ or vice versa.

polyA polymerase. The enzyme that adds the polyA tail at the 3′ end of eukaryotic mRNA molecules.

polyadenylation signals. A specific sequence (AAUAAA) in a nascent eukaryotic mRNA that specifies the site for endonucleolytic cleavage of the transcript and addition of the polyA tail.

polycistronic mRNA. An mRNA molecule that contains multiple open reading frames, usually found in prokaryotic mRNAs.

polyclonal. Refers to an antiserum containing a number of different types of antibody molecules directed against various determinants on an antigen. These antibodies are secreted by various B cells, each derived from a distinct precursor by clonal selection.

polydnavirus. A DNA virus replicating in the ovaries of certain parasitic wasps that can suppress the immune response of the caterpillar prey to the developing wasp embryo.

polymerase chain reaction (PCR). A linked set of reactions using sequence-specific primers and a high-temperature DNA-dependent DNA polymerase; used to amplify a specific DNA sequence by multiple rounds of primer-directed DNA synthesis.

polythetic. Defining the relationships between members of the groups based on several similarities rather than a single, common feature.

positive-sense RNA. RNA whose sequence is the sense of mRNA.

positive-sense RNA virus. A single-stranded RNA virus whose genome is the same sense as mRNA.

positive strand. See **positive sense**.

positive (+) strand viruses. A Baltimore scheme classification of viruses that have positive-sense RNA genomes.

posttranscriptional modifications. Cellular enzymatic modifications to the primary structure of a transcript following synthesis from the DNA (or RNA) template; include polyadenylation, capping, and splicing.

poxviruses. Family of large, dsDNA genome viruses that replicate in the cytoplasm of their host cells.

pre-biotic. Referring to the time in the history of the earth before the existence of cellular forms of life, or before the existence of living structures, such as self-replicating molecules.

pre-initiation complex. The assembly of transcription factors and RNA polymerase II at the TATA box and cap site of a eukaryotic transcript that forms just prior to the initiation of transcription.

Pribnow box. An AT-rich sequence 10–12 base pairs upstream of the start site of prokaryotic transcription that serves as an association site for RNA polymerase; analogous to the TATA box of eukaryotic mRNA.

primary cells. Cells isolated directly from the tissue of origin that display all the histological and growth properties of cells in the tissue of origin.

primase. The enzymatic activity that catalyzes the synthesis of the RNA primer that begins DNA replication.

primosome. The complex of primase and DNA helicase that is involved in the synthesis of the RNA primer for DNA replication.

prion. An infectious agent spread by ingestion that does not appear to contain any genetic material. It is thought to be a host cell protein that is folded in such a way as to lead to neurological degeneration and can induce similar conformational changes in identical proteins originally folded in a benign manner in the infected individual.

procapsid. A precursor to a mature viral capsid.

prodromal period. A time prior to the onset of full symptoms of a disease when specific physiological responses resulting from it can be discerned by a practiced observer.

productive infection. A virus infection of cells in which more infectious virus is produced than was present to initiate the infection.

professional antigen presenting cells. Cells of the immune system whose function is to take up antigens by endocytosis, degrade them into fragments, and display the fragments on their surface in complex with class II MHC. Such cells include macrophage and B lymphocytes.

programmed cell death. See **apoptosis**.

promoter. A region of DNA proximal to the transcript start site of a gene that controls the formation of the pre-initiation complex and transcription.

propagate. Spread by replication.

prophage. The form of the genome of a lysogenic bacteriophage integrated into the host cell chromosome.

prophylactic. Preventative.

***prot* (*protease*).** The gene expressed by a number of viruses, especially retroviruses, that catalyzes the proteolytic maturation of polyproteins into specific virus proteins.

proteome. The dataset of all proteins encoded by and expressed from a genome or set of sequences.

proteosome. A complex structure within eukaryotic cells that is the site of protein degradation. Proteins destined for turnover at the proteosome have been tagged by the addition of **ubiquitin**.

prototrophy. The ability of bacteria to grow and replicate with only an energy and carbon source (usually a sugar) and inorganic sources of nitrogen, sulfur, and phosphorus.

provirus. The double-stranded cDNA produced by reverse transcriptase as the first step in infection by a retrovirus.

pseudo-pregnant female. In the production of a **transgenic mouse**, a female mouse of breeder age that has been hormonally treated to make her receptive to receive an embryo.

pulse. As applied to a virus infection or other molecular and biochemical applications, a short time interval in which an experimental modification of conditions such as the addition of a radioactive precursor is carried out.

pulse-chase experiment. An experimental protocol in which a radioactive precursor is provided to a system for a defined, usually short, amount of time, which is then followed by the addition of a large excess of unlabeled precursor (chase) to dilute the pool of material; used to follow the fate of material synthesized during the pulse period.

quantal assay. A statistical assay of infectious virus based on dilution endpoints.

quasi-species swarm. A population of RNA viruses in which, by random errors made during genome replication, a large number of possible variants are represented, for instance, any population of HIV particles.

R-loop mapping. A method of visualizing genes using electron microscopy to detect the looping out of DNA from an RNA-DNA duplex formed by the hybridization of mRNA and the double-stranded DNA gene encoding it.

random reassortment. The random mixing of genomic segments following mixed infection with a virus with a segmented genome; an important mechanism for generating genetic diversity in reoviruses and influenza viruses.

rate zonal centrifugation. A technique of subjecting a macromolecule, organelle, or virus particle to a high centrifugal field so that its rate of sedimentation allows it to be separated from other materials that have different sedimentation rates (see also **centrifugation**).

reactivation (recrudescence). Periodic reappearance of an infectious agent following a period of latency; a hallmark of herpesvirus infections.

real time PCR. A method for the quantitative detection of amplified products of **PCR**. Real time PCR measures the increase in copy number during early stages of the amplification process, using fluorescent reaction components. This is in contrast to traditional PCR, which is an endpoint analysis.

reanneal. To allow the two complementary strands of a double-stranded nucleic acid that have been separated (denatured) by chemical or thermal denaturation to re-form the original duplex.

receptor. A specific macromolecule (usually a protein) on the surface of a cell that interacts with one or several specific proteins present in the exterior medium. In the case of a virus infection, the cellular receptor interacts with a specific viral structural protein or proteins to initiate infection.

recombinant. See **genetic recombination**.

recrudescence. A new outbreak of symptoms after a time during which symptoms were absent or greatly reduced.

reovirus. Viruses with a segmented, dsRNA genome.

replica plate. A method of replicating an organism or virus on a solid or semisolid surface so that the spatial relationship between individual clones is maintained for screening or selection.

replication fork. The growing point in the replication of a DNA duplex molecule.

replicative intermediate (RI). The replicating structure, consisting of a template strand and multiple complementary progeny strands, found in cells infected with a single-stranded RNA virus. There are two forms: RI-1 is the complex synthesizing complementary strands using virion (genomic) or virion-sense RNA as a template; RI-2 contains RNA complementary to genomic RNA as the template and genomic-sense RNA as the product strands.

replicon. A region of DNA or RNA genome whose replication is controlled by an **origin of replication (ori).**

reporter gene. A gene not normally found within a eukaryotic cell whose expression can be used as a measure of gene expression in that cell. Chloramphenicol acetyl transferase (CAT) is a bacterial enzyme that can be used in this way for the study of gene expression in eukaryotes.

repressor. A regulatory protein that blocks the expression of a gene by binding to a specific regulatory sequence in the DNA encoding it.

reservoir. The source of an infectious agent.

resolvase. An enzyme that can convert DNA recombination intermediates, such as the Holliday structure, to separate molecules by endonucleolytic scission and rejoining.

restriction enzyme. A DNA endonuclease that is expressed in bacterial cells in order to degrade foreign DNA. The recognition sites are often palindromic, and various specific restriction endonucleases recognize exact double-stranded DNA sequences of 4 to 8 bases. The ability to cleave large pieces of DNA into specific fragments with such enzymes is an important basic tool in molecular cloning methods.

retroelements. Regions of genomic DNA that contain structures such as long terminal repeats and genes for expressing reverse transcriptase and other enzymatic functions seen in retroviruses. Retrotransposons are one type of retroelement.

retrotransposon. Transposable DNA sequences in eukaryotic cells that replicate using RNA intermediates and reverse transcriptase. Retrotransposans are also called Class I transposons.

reverse genetics. The reverse of traditional genetics. Rather than starting with a phenotype or gene product and searching for a gene, the experimenter begins with a region of known DNA sequence and then seeks to discover the phenotype or product of the presumed gene.

reverse transcriptase (Pol). An enzyme, originally discovered in retroviruses, that uses single-stranded RNA as a template for the synthesis of a cDNA sequence; can also use DNA as a template, and can degrade RNA from a DNA–RNA hybrid. This latter activity is termed RNase H activity.

reverse transcription-polymerase chain reaction (RT-PCR). A PCR reaction performed in conjunction with, or following a reverse transcription reaction for detecting and quantifying small amounts of RNA. The reverse transcription reaction (catalyzed by the enzyme reverse transcriptase) synthesizes a cDNA copy of the RNA. The PCR reaction then amplifies specific cDNA sequences, depending on the primers used.

RI-1 (RI-2). See **replicative intermediate**.

ribonucleoprotein (RnP). A complex of RNA and protein; see **nucleoprotein**.

ribosomal RNA (rRNA). The RNA species that make up structural and, in one case, enzymatic portions of both prokaryotic and eukaryotic ribosomes.

ribozyme. An enzymatic activity of certain RNA molecules, such as the self-splicing of plant viroid RNA.

RIG-1. Retinoid-inducible gene 1. RIG-1 is a negative regulator of cellular growth that can induce differentiation or apoptosis.

RNA-dependent transcriptase. An enzyme synthesizing RNA (usually mRNA) using Watson–Crick base-pairing rules and RNA as a template.

RNA editing. An enzymatic change in the sequence of RNA by directly changing one of the bases. The process occurs in the replication of hepatitis delta virus as well as in the biogenesis of plant mitochondrial mRNA.

RNase-H. A ribonucleolytic activity of the reverse transcriptase enzyme that degrades the RNA portion of an RNA–DNA hybrid.

RNase-L. A ribonucleolytic activity that degrades mRNA when induced by 2′,5′-oligoadenylate in the presence of dsRNA; part of the antiviral state induced by interferon.

RT-PCR. See **reverse transcription-polymerase chain reaction**.

R:U$_5$:(PB):leader region. The 5′ terminal region of a retrovirus genome, containing a sequence also present on the 3′ end (R), a sequence unique to the 5′ end (U5), a binding site for the tRNA primer of replication (PB), and an untranslated region between PB and the first open reading frame (leader).

rubella. German measles.

s value. A numerical measure of the sedimentation rate of a macromolecule, organelle, or virus when the material is subjected to high centrifugal fields under defined conditions.

sarcoma. A malignant solid tumor of mesodermal cells, such as muscle.

SARS. See **Severe acute respiratory syndrome.**

scaffolding proteins. Proteins that are involved in the assembly of a viral capsid but are not part of the mature virion.

scale-free network. A network in which a small percentage of nodes are connected to large numbers of other nodes. Such networks are called "scale-free" because their topography appears the same at any level of resolution (scale).

SCID mouse. Severe combined immune-deficient mouse. These animals are useful in experimental models and have been specifically bred so that they lack both T-cell and B-cell immunity.

scrapie. A slow, progressive, prion-caused neurological disease of sheep that leads to paralysis and death.

screen. To isolate manually or automatically a desired mutant or cell line using observable differences between the desired phenotype and the background.

segmented genome. A viral genome existing as two or more separate segments of nucleic acid; for example, the genome of influenza viruses.

select. To isolate a desired genotype by incubating it and other genotypes under conditions where only the desired entity can replicate efficiently.

selectable genetic marker. A genetic element whose presence within a particlar genome allows for selection of that genome during experimental manipulations.

selfish genes. Genes whose only function is to replicate themselves, providing no advantage to the entity carrying them; originally defined by Francis Crick to explain the existence of certain self-replicating genetic elements.

semipermissive. A condition in which the infected cell functions as a poor host for the virus, resulting in a very low production of progeny.

senesce. To age to infirmity; in the case of normal cells in culture, the gradual loss of the ability to divide after multiple serial passages.

sequela (ae). The long-term consequence of a disease.

serotype. An organism or microbe with a distinct immunological signature.

severe acute respiratory syndrome (SARS). An emerging viral disease that presented first in Southeast Asia and China, followed by an outbreak in Canada. The disease, characterized by acute pulmonary edema, is caused by a coronavirus.

sex pilus. One of the projecting portions of the bacterial cell wall that can instigate mating with a bacterial cell of another sex; used as a receptor by male-specific bacteriophages.

Shine–Dalgarno sequence. A sequence element in prokaryotic mRNA, discovered by John Shine and Lynn Dalgarno, that binds to 16S rRNA and signals the site of initiation of translation at the nearest AUG downstream.

shingles. Clinical manifestation of latent infection by varicella-zooster virus, a member of the human herpesvirus group. The initial infection is chickenpox, followed by years of latency, and then expression of shingles as a painful recrudescence on the surface of the skin.

signal transduction cascade. A series of reactions, precipitated by the binding of a factor to a cellular receptor. The series, which may involve phosphorylations, as an example, results in the activation of a final regulatory molecule, such as a transcription factor.

signaling cascade (see signal transduction cascade)

small interfering RNAs (siRNAs). Small (21-nt) double-stranded RNAs produced from larger dsRNA by the action of **dicer**. siRNA unwinds and interacts with RISC (RNA-induced silencing complex) to bind to specific mRNAs and degrade them, thus silencing the production of protein from that gene.

smallpox (variola). The first human viral disease to be eradicated from the population; caused by a cytoplasmic DNA virus. The disease had two forms caused by different viral serotypes: variola major was the most severe form while variola minor was a form characterized by a lower death rate and generally milder symptoms.

snRNA. One of a class of small nuclear RNAs of eukaryotic cells involved in splicing; functions with cognate proteins to form a nuclear organelle termed a *small nuclear ribonucleoprotein particle* or snRNP.

Southern blot. Transfer of DNA, separated by agarose gel electrophoresis, to nitrocellulose membranes by blotting. Named after the developer, Edward Southern.

spliceosomes. The nuclear organelles made up of snRNA, unspliced pre-mRNA, and specific proteins that are formed as the first step in the splicing reaction of eukaryotic mRNA.

splicing. The process of removing interior segments (introns) of eukaryotic pre-mRNA as part of posttranscriptional modification.

ssDNA-binding protein. A protein involved in DNA replication that prevents reannealing of the two denatured strands at the replication point by binding to the single-stranded DNA in a sequence-independent manner.

SSPE. See **subacute sclerosing panencephalitis**.

stimulation index. A quantitative measure of T-cell proliferation in response to stimulation by a recognized antigen.

stochastic. Random.

strong stop. A step in the transcription of a retroviral genome into cDNA by reverse transcriptase; occurs after synthesis of cDNA from the tRNA primer to the 5′ end of the genome and is a result of translocation of the newly synthesized cDNA strand to the other end of the RNA template.

structural protein. A viral protein that is normally found specifically associated with the infectious virus particle.

subacute sclerosing panencephalitis (SSPE). A rare autoimmune disease caused by the host immune system destroying neural tissue in which noninfectious measles virus is maintained

following recovery from the acute phase of infection; usually occurs within 5 years of the initial infection.

subcutaneous. Under the skin.

subgenomic mRNA. An RNA transcript of an RNA viral genome that contains only part of the sequence present in the entire genome.

subunit vaccine. A vaccine preparation that contains only a viral antigenic protein.

suppression. Change in the phenotype of a mutant by the effect of a mutation in a different gene, negating the effect of the original mutant.

symmetry. Arrangement of repeating subunits in a structure; refers to the arrangement of virus capsomers within the virion.

symptoms. Diagnostic features of a disease.

syncytia. Cells whose cytoplasm has fused; one type of cytopathology induced by infection with some viruses.

syndrome. A set of symptoms characteristic of a specific disease. This term is often used to describe a long-lasting condition.

systemic immune response. The host defense component that involves a system-wide response, including both humoral and cell-mediated immunity.

T (large T) antigen. The autoregulatory multifunctional early protein expressed by papovaviruses that functions to initiate rounds of viral DNA replication, inactivate cellular tumor suppressor genes, and activate late transcription.

t (small t) antigen. The early protein colinear with the N-terminal portion of T antigen expressed during infection with polyomaviruses. Its function is dispensable for virus replication in cultured cells.

T helper 1 cells (Th1). A subset of T-helper cells. Th1 cells suppress the activity of **Th2** cells and produce IL-1, IL-2, γ-interferon, and TFN-β. Th1 cells activate macrophage, assist B-cells, and are involved in delayed hypersensitivity.

T helper 2 cells (Th2). A subset of T-helper cells. Th2 cells secrete a variety of interleukins, as well as being involved in a number of features of cell-mediated immunity.

T lymphocytes. Immune cells that react with other cells bearing foreign antigens on their surface due to viral infection or genetic alteration.

TAP. Transporter associated with **a**ntigen **p**rocessing. Transport proteins responsible for moving fragments of antigens into the Golgi prior to presentation in complex with MHC I.

target tissue (organ). The tissue or organ of an individual infected with a pathogen that, when infected, is responsible for the appearance of the characteristic symptoms of the disease.

TATA box. The AT-rich region (canonical sequence TATAA) about 25 base pairs upstream of the cap site of eukaryotic transcripts that serves as the nucleation point for the assembly of the pre-initiation transcription complex.

TATGARAT sequence. The nominal 8-base sequence in double-stranded DNA to which the Oct1 and related proteins bind. In HSV-1 these elements occur in the enhancers for the immediate-early gene promoters, and the binding of Oct1 leads to subsequent association with the α-TIF protein and transcriptional activation.

$TCID_{50}$. Median tissue culture infectious dose; in a quantal assay, the dilution at which half the tested aliquots are able to initiate an infection in a test culture of cells, i.e., contain an infectious virus particle or PFU.

tegument. The matrix of proteins and other material between the capsid and envelope of a herpesvirus virion.

telomere. A structural element at the end of a eukaryotic chromosome that contains multiple repeated DNA sequences and a closed end.

temperature-sensitive (ts) mutation. A conditional lethal mutation where an altered protein cannot assume its correct folding and structure at a high (nonpermissive) temperature and,

thus, cannot function. At a lower (permissive) temperature, the protein can assume its correct structure and function normally.

termination factor (ρ factor). A protein that is involved in the termination of transcription of one class of prokaryotic mRNA molecules.

therapeutic index. A numerical measure of the effectiveness of a drug or therapeutic method. It is most simply the ratio of some numerical measure of the effectiveness against the disease or infectious agent to a measure of undesirable side effects.

thymidine kinase (TK). An enzyme involved in the salvage of pyrimidines within the cell; encoded by a number of herpesviruses and some other large DNA viruses.

tissue tropism. The property of a virus that allows it to grow in a specific tissue.

titer. Quantitative measure of the amount of a medically important substance or entity.

"toll-like" receptor (TLR). Transmembrane proteins that are involved in pathogen recognition and activation of both the innate and adaptive immune response. TLRs are so named because of homology to the *Drosophila toll* gene product.

topoisomerase. An enzyme that can change the superhelicity of a double-stranded DNA molecule.

***trans*-acting genetic elements.** Genetic elements, transcripts, or proteins functioning throughout the cell in which it is expressed; the converse of a *cis*-acting element, which only functions on elements within the contiguous genome in which it occurs.

transcription. The enzymatic synthesis of RNA from either a complementary DNA or RNA template.

transcription factors. A group of nuclear proteins of eukaryotes involved with RNA polymerase in the transcription of RNA from a DNA template. Many transcription factors are able to bind to specific sequences within the promoters and other regulatory regions of transcripts.

transcription-termination/polyadenylation signal (cleavage/polyadenylation signal). A sequence of bases that occur over 25–100 base pairs at the 3′ end of the gene encoding a specific transcript that signals the point at which the RNA polymerase disassociates from the template. A major feature of this region is the presence of one or more sequences that are templates for polyadenylation signals in the transcript.

transcriptome. A database of all transcribed sequences of a particular genome.

transfection. The process of introduction of nucleic acid into a cell by nonspecific chemical means.

transfer blot. One of three methods (Southern, northern, or western) for transferring molecules that have been separated by gel electrophoresis to nitrocellulose or similar membranes. The process uses a blotting procedure to move the molecules out of the gel and onto the membrane surface.

transfer vector. Also called gene transfer vector, a viral vector designed to transfer a gene to a cell or tissue for **gene therapy** purposes.

transformation. The alteration of a cell by insertion of one or more foreign or mutant genes.

transgene. A foreign gene that has been inserted, using recombinant DNA technology, into a genome and that can be expressed from that position.

transgenic mouse. A mouse that has been engineered to express a foreign **transgene**. This gene can be from a virus, another organism, or a reporter gene.

transitory (transient or abortive) transformation. The change of a cell's growth characteristics by the temporary expression of a transforming gene product without a genotypic change in that cell; a temporary state of transformation, such as with a nonintegrating plasmid.

translocation. In virus infection, the process of the genome-containing portion of the virion being biochemically transported across the cell or nuclear membrane.

transposase. An enzyme mediating transposition of a transposable genetic element.

transposon. A genetic element that can move by recombination from one location to another in a genome; often encodes genes that catalyze transposition.

tropism. The tendency of a virus or other pathogen to favor replication in a specific set of tissues or site in the body.

tumor antigen (T antigen). Generally, an antigen found on or in a tumor but not a normal cell; specifically an early multifunctional protein expressed by polyomavirus and SV40.

tumor suppressor genes. Cellular genes whose function is to block uncontrolled cell replication.

ubiquitin. A small (76 amino acid) protein in eukaryotic cells that is covalently linked to proteins destined for degradation at the **proteosome**.

VA RNA. One of two small (about 160 nucleotides) transcripts transcribed early from the adenovirus genome by host RNA polymerase III; responsible for inhibiting the effects of interferon-α and interferon- β.

vaccination. The process of using an inactivated or attenuated pathogen (or portion thereof) to induce an immune response in an individual prior to his or her exposure to the pathogen.

varicella zoster virus (VZV). A member of the Herpesvirus family that is the causative agent of chicken pox during acute infection and, after a period of years, of shingles as a consequence of the latent infection.

variola. See **smallpox.**

variolation. The practice of injecting dried exudate from recovering smallpox patients into an immunologically naive individual in order to generate protective immunity.

vector. The agent or means by which an infectious agent is spread from one individual to another; also refers to an engineered plasmid or virus designed to transfer genes into an organism.

vegetative DNA replication. Exponential viral genome replication.

vesicle. A membrane-bound cellular compartment; also a fluid-filled blister or pouch that contains the infectious agent during an infectious disease.

viral cloning vector. A cloning vector based upon the genome and replication strategy of a particular virus.

viremia. The presence of a virus in the blood and circulatory system.

virion. A virus particle that appears structurally complete when viewed in the electron microscope.

viroid. A plant pathogen that is the smallest known nucleic acid-based agent of infectious disease. Each is a 250- to 350-base circular RNA molecule that encodes no protein and is not encapsidated. Hepatitis delta virus shares some features of viroids, including a highly structured circular RNA genome.

virosphere. The complete array of viruses present in the biosphere.

virulence. A measure of the severity of the disease-causing potential of a pathogen.

virus passage. Transmission and generation of virus stocks by multiple rounds of virus replication, usually in the laboratory.

Watson–Crick base-pairing rules. The basic rules that describe how one strand of a double-stranded nucleic acid can specify the sequence of the complementary strand; named for the two scientists who formally proposed them based on chemical and x-ray crystallographic data of double-stranded DNA. Most simply stated: (i) A pairs with T (or U in RNA), G pairs with C; and (ii) the two strands are antiparallel.

western blot. A method for transferring proteins that have been separated by gel electrophoresis to a nitrocellulose membrane by blotting. So named with reference to the Southern and northern blot transfer techniques.

xenograft. A piece of tissue or organ from a different species that is implanted or transplanted into an animal.

x-ray crystallography. The determination of structure at the atomic level by the analysis of x-rays that are reflected from the planes of a crystal prepared from a macromolecule or virus particle.

yeast artificial chromosome (YAC). A cloning vector constructed to be a self-replicating element in yeast cells. The YAC contains the centromeric region, origin of replication, and telomeres from a yeast chromosome. YACs have very large (up to 1000 kbp) cloning capacities.

zoonosis. A virus disease of another animal species that can cause a human disease.