

# Glossary

**Amino Acids:** The building blocks of proteins. The unique sequence of amino acids in a chain defines the character of a protein molecule.

**Angiogenesis:** The process by which the body forms and develops new blood vessels. Angiogenesis can be both beneficial and harmful; while it can be used to stimulate development in new blood vessels to fight clogged arteries, it also allows malignant tumors to increase in size. Angiogenesis is a key area of cancer research.

**Antibody:** A component of the body's immune response. A Y-shaped protein, it is secreted in response to an antigenic stimulus. It neutralizes the antigen by binding to it.

**Antigen:** Any substance, almost always a protein, not normally present in the body that when introduced to the body stimulates a specific immune response and the production of antibodies.

**Apoptosis:** The process of programmed cell death that may occur in multicellular organisms. Programmed cell death involves a series of biochemical events leading to characteristic cell changes and death. Apoptosis is a key area of cancer research.

**Aseptic:** Describes a product or method free of microbiological organisms that would lead to contamination.

**Assay:** A test procedure whereby a property or concentration of a substance is measured.

**Autoimmune Disorders:** Diseases whereby an individual's immune system mounts an attack on a portion of its own tissues. Tissues undergoing such an attack can be destroyed in the process.

**Base Pairs:** Two nucleotides on opposite complementary DNA or RNA strands that are connected via hydrogen bonds. In DNA, adenine (A) forms a base pair with thymine (T), as does guanine (G) with cytosine (C). In RNA, thymine is replaced by uracil (U).

**Bioinformatics:** The application of information technology to the field of molecular biology. Bioinformatics entails the creation and advancement of databases, algorithms, computational

and statistical techniques, and theory to solve formal and practical problems arising from the management and analysis of biological data.

**Biologic:** A product derived from a living organism (from animal products or other biological sources) that is used in the diagnosis, prevention or treatment of disease. Examples of biologics include recombinant proteins, allergy shots, vaccines and hematopoietic growth factors.

**Biologic License Application:** An application filed with the FDA seeking approval to market a novel biologic in the United States. The application contains a description of the trials and results, formulation, dosage, drug shelf life, manufacturing protocols, packaging information, etc.

**Biomarker:** A substance used as an indicator of a biologic state. It is a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes or pharmacologic response to a specific therapy. Biomarker identification and measurement are regarded as key developments for the future of disease treatment. Biomarkers are also used in drug discovery to determine whether a drug is effective in animal models and at what doses effectiveness is reached.

**Biopharmaceutical:** A synthetic drug produced utilizing certain biotechnology methods.

**Bioreactor:** A device or system for growing cells or tissues in the context of cell culture. The process of fermentation is performed in a bioreactor to grow large volumes of cells for producing specific proteins.

**Biosensor:** A device that combines a biological component with a physicochemical detector component to detect a pathogenic agent.

**Biotechnology:** Technology based on biology, especially when used in agriculture, food science and medicine. The United Nations Convention on Biological Diversity defines biotechnology as "any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use."

**Blood-Brain Barrier:** A physiological mechanism that alters the permeability of brain capillaries so that some substances, such as certain drugs or toxins, are prevented from entering brain tissue, while other substances are allowed to enter freely.

**Cell Bank:** A facility where cell lines are kept frozen and stored for later use. Cell banks include master cell banks (MCBs) and working cell banks (WCBs). MCBs house primary cell strains that are kept stored and not used for production purposes. WCBs house cells used in pharmaceutical production grown from those maintained in an MCB so that their stability and uniformity are well characterized.

**Cell Culture Technology:** The growing of cells outside of living organisms. With mammalian cell culture, it is sometimes possible to replace animal testing with cell testing when evaluating the safety and efficacy of medicines.

**Cell Lines:** Generations of cells grown from original primary cells. Primary cells are cultured directly from a living organism. With the exception of some derived from tumors, most primary cell cultures have limited life spans. After a certain number of population doublings, cells usually stop dividing, though they remain alive. An established or immortalized cell line has acquired the ability to proliferate indefinitely through either random mutation or deliberate modification.

**Cell Viability:** Determining whether a cell population is living or dead. Testing for cell viability usually involves looking at a sample cell population and staining the cells or applying chemicals.

**Chemical Library (or Compound Library):**

A collection of stored chemicals that may be used in high-throughput screening for drug development. The larger the chemical library, the better the chance that high-throughput screening will find a hit (a potential drug candidate).

**Chinese Hamster Ovary Cells (CHO cells):** A cell line often used in biological and medical research, first introduced in the 1960s. CHO cells are used in studies of genetics, toxicity screening, nutrition and gene expression, particularly expression of recombinant proteins. CHO cells are the most commonly used mammalian hosts for industrial production of protein therapeutics.

**Chromatography:** A process by which complex

mixtures of different molecules may be separated from each other. This is accomplished by subjecting the mixture to many repeated partitionings between a flowing phase and a stationary phase.

**Chromosome:** A threadlike linear strand of DNA and proteins in a cell that houses genes. Chromosomes are large enough to be seen under a microscope. In humans, all cells other than germ cells usually contain 46 chromosomes: 22 pairs of autosomes and either a pair of X chromosomes (in females) or an X chromosome and a Y chromosome (in males). In each pair of chromosomes, one chromosome is inherited from the father and one from the mother.

**Clarification:** A step in the downstream phase of manufacturing a biologic. After the protein product is harvested, which may include removing intracellular proteins from cells, clarification steps separate the protein from cellular debris. Individual proteins are then separated using chromatography methods.

**Clinical Trial:** A type of research study that evaluates the safety and efficacy of new drugs, medical devices and biologics in human subjects. These tests are required by regulatory agencies as a precondition of regulatory clearance to market.

**Cloning:** The replication of a DNA sequence from one organism to create an exact genetic copy; processes used to create copies of DNA fragments (molecular cloning), cells (cell cloning) or organisms.

**Codon:** A string of exactly three mRNA bases that code for a specific amino acid during translation of mRNA into DNA.

**Colony Hybridization:** The screening of a library with a labeled probe (radioactive, bioluminescent, etc.) to identify a specific sequence of DNA, RNA, enzyme, protein or antibody.

**Column Chromatography:** A type of chromatography that uses a column for containing and separating a mixture. It is a commonly used method of purifying proteins.

**Combinatorial Chemistry:** A discipline in which a large number of new chemicals are created, compiled into a library and screened for potential therapeutic use.

**Cryopreservation:** A process whereby cells or whole tissues are preserved by cooling to low subzero temperatures. At these low temperatures, any biological activity, including the biochemical reactions that would lead to cell death, is effectively stopped.

**DNA (Deoxyribonucleic Acid):** DNA is a nucleic acid that contains the genetic information used in the development and functioning of all organisms. Molecular systems interpret the sequence of these nucleic acids to produce proteins.

**DNA Fingerprinting:** A technique used to distinguish between individuals of the same species using only samples of their DNA.

**DNA Ligase:** The enzyme that creates a bond between the ends of single-stranded DNA segments. Where restriction enzymes are the scissors of recombinant DNA technology, DNA ligase is the glue.

**DNA Polymerase:** An enzyme that attaches complementary nucleotides to a single stranded human DNA.

**DNase (Deoxyribonuclease):** Any enzyme that catalyzes the breaking up of linkages in the DNA molecule backbone.

**Downstream Phase:** Involves manufacturing processes including the recovery, purification, formulation and packaging of the protein.

**Enzyme-Linked Immunosorbent Assay (ELISA):** A biochemical technique to detect the presence of an antibody or an antigen in a sample. It is commonly used to detect infectious agents.

**Enzymes:** The many proteins produced by organisms to act as biochemical catalysts. Enzymes are the mediators of cell metabolism.

**Epidermal Growth Factor Receptor (EGFR):** A cell-surface receptor that is activated when bound by epidermal growth factor. Genetic mutations that lead to EGFR overexpression or overactivity have been associated with a number of cancers.

**Extracellular Proteins:** Proteins found outside of a cell.

**Fermentation:** A process of growing, or culturing, cells by using enzymes to effect chemical changes.

**Fusion Proteins (or Chimeric Proteins):** Proteins created through the joining of two or more genes that were originally coded for separate proteins. Translation of this fusion gene results in a single new protein with functional properties derived from each of the original proteins.

**Gel Electrophoresis:** A technique used for the separation of DNA, RNA or protein molecules by using an electric current applied to a gel matrix. The gel is the medium used to contain, then separate the target molecules. *Electrophoresis* refers to the use of electricity to move the molecules through the gel matrix. Placing the molecules in wells in the gel and applying an electric current moves the molecules through the matrix at different rates based on their size, charge and/or shape.

**Gene:** A length of DNA that codes for a particular protein or, in certain cases, a functional or structural RNA molecule.

**Generally Regarded as Safe (GRAS):**

A designation that a substance is considered safe by experts under the conditions of its intended use. Examples are CHO and NS0 cell lines that have GRAS status for therapeutic protein production.

**Genetic Engineering:** Alteration of the genetic material of cells or organisms in order, for example, to make them capable of making new substances or performing new functions.

**Glycosylation:** The process by which oligosaccharide units are added to proteins.

**Half-life:** A measurement of the time it takes for a drug to lose half of its pharmacologic activity or half of its administered amount in the bloodstream or in its target tissues.

**Hematopoietic Growth Factors:** Protein hormones produced by the body to regulate blood development, affecting the production and maturation of blood-forming cells.

**High-Throughput Screening:** The process of screening a sample of compounds rapidly and in parallel, then analyzing the results and choosing further screening compounds based on this information.

**Hormones:** Substances produced by one tissue and conveyed to another through the bloodstream, usually affecting growth or metabolism.

**Humanized Antibodies:** Monoclonal antibodies that have been synthesized by using recombinant DNA technology to avoid the clinical problem of an immune response to foreign substances. Humanized antibodies are produced by merging the DNA that encodes the binding portion of a monoclonal mouse antibody with human antibody-producing DNA. Cell cultures are used to express this recombinant DNA and produce these partial-mouse and mostly human antibodies.

**Hybridization:** The process of joining two complementary strands of DNA or one each of DNA and RNA to form a double-stranded molecule.

**Hybridoma:** A cell that has been engineered to produce a desired antibody in large amounts. Hybridomas are created by fusing immortal tumor cells with antibody-producing B-lymphocyte cells that continuously synthesize identical (or monoclonal) antibodies.

**Immortal Cell Line:** An established cell line that has acquired the ability to proliferate indefinitely through either random mutation or deliberate modification.

**Immunotherapy:** Modulation of the immune system to achieve a therapeutic goal. Monoclonal antibodies are a type of immunotherapy.

**Interferon:** A naturally occurring cell-signaling protein produced by the immune system in response to infections such as viral infections or parasites.

**Intracellular Proteins:** Proteins found inside a cell.

**Investigational New Drug:** A drug that has been approved by the FDA for use in human clinical trials.

**In vitro:** The technique of performing an experiment outside of a living organism, in a controlled environment such as in a cell culture or in cells grown in a petri dish.

**Ion Channels:** Pore-forming proteins that help establish and control the small voltage gradient across the plasma membrane of all living cells. Ion channels are involved in a wide variety of biological processes and are a favorite target in the search for new drugs.

**Mass Spectrometry (MS):** An analytic technique for determination of the elemental composition of a sample or molecule. It is also used for de-

termining the chemical structures of molecules, such as peptides or proteins. MS consists of ionizing chemical compounds to generate charged molecules or molecule fragments, then measuring their mass-to-charge ratios.

**Media:** Nutrient-rich substances in which cells are grown.

**Messenger RNA (mRNA):** A polynucleotide copy of a DNA gene that communicates the code for building a protein to ribosomes so that new proteins can be built.

**Microarray:** A tool that enables analysis of the levels of expression of genes in an organism or comparison of gene-expression levels.

**Monoclonal Antibody:** An antibody produced by cells that are all derived from a single antibody-producing cell. Once a cell capable of generating an antibody with desired therapeutic characteristics is selected, laboratory processes are used to clone (make large numbers of) these cells. Since the cells are all identical and are produced by cloning one specific cell in great numbers, they are called monoclonal and can be used to continuously produce identical antibody molecules with these same therapeutic characteristics.

**Nanomedicine:** The medical application of nanotechnology.

**Nanotechnology:** The study and creation of systems and devices at the level of molecules and atoms.

**Neurotransmitters:** Chemicals that are used to relay, amplify and modulate signals between a neuron and another cell.

**Non Secreting (NS0) Cells:** Mouse myeloma cells that are used frequently in the production of recombinant antibodies.

**Nucleotide:** The name given to an individual unit of the DNA double helix and RNA. A nucleotide contains one sugar, one phosphate and one base.

**Nucleus:** The organelle within a living cell that contains genetic material and controls life functions.

**Pathogen:** A disease-causing agent such as a bacterium or virus.

**Pegylation:** The process of adding polyethylene glycol to a therapeutic protein, which enables

the therapeutic protein to stay in the body longer.

**Peptibodies:** Engineered therapeutic fusion proteins with attributes of both peptides and antibodies but that are distinct from each and that can bind to human drug targets.

**Peptide Bond:** A bond that links together two or more amino acids. A protein is a long chain of amino acids joined together with peptide bonds and therefore is sometimes referred to as a polypeptide.

**Peptides:** Short chains of amino acids. Polypeptides, or multiple peptides linked together by peptide bonds, are long chains of amino acids.

**Personalized Medicine:** Use of the information contained within a patient's genome, genotype or genomic signature to design and tailor the best treatment plan for that individual patient.

**Pharmacodynamics:** Studies performed to determine what a drug does to the body.

**Pharmacogenomics:** The science of understanding the correlation between patients' genetic makeup (genotype) and their responses to drug treatment.

**Pharmacokinetics:** Studies performed to determine what the body does to a drug.

**Phosphorylation:** The addition of a phosphate ( $\text{PO}_4$ ) group to a protein or other organic molecule. Protein phosphorylation plays a significant role in a wide range of cellular processes.

**Polymerase Chain Reaction (PCR):** A method for creating millions of copies of a particular segment of DNA. If a scientist needs to detect the presence of a very small amount of a particular DNA sequence, PCR can be used to amplify the amount of that sequence until there are enough copies available to be detected.

**Preclinical Trials (or Studies):** Tests that take place in a scientifically controlled setting using cell culture and/or animals as disease models.

**Product Pipeline:** In the biomedical industry, the term *pipeline* refers to the number of unique products or processes reported or in development by a company. Drugs that have entered into clinical trials are said to be "in the pipeline."

**Protein Engineering:** A process for isolating and studying proteins and generating proteins with

modified structures by altering the genes that direct their composition.

**Proteins:** Compounds (chains of amino acids) constituting the ultimate expression product of a gene. Created through the synthesis performed by ribosomes, proteins are the workhorses of living systems, causing chemical processes and changing as their environment changes.

**Proteomics:** The study of proteins. Proteomics has three major goals: to identify and quantify all the proteins expressed in an organism, to determine the structure and function of each protein and to study the protein-protein interactions that affects how one protein interacts with other proteins to control cellular processes.

**Receptor (Cell Receptor):** A protein molecule, embedded in either the plasma membrane or the cytoplasm of a cell, to which a mobile signaling (or signal) molecule may attach. A molecule that binds to a receptor is called a ligand, and may be a peptide (such as a neurotransmitter), a hormone, a pharmaceutical drug or a toxin, and when such binding occurs, the receptor goes into a conformational change, which usually initiates a cellular response.

**Recombinant DNA:** A form of DNA that does not exist naturally and is created by combining DNA sequences that would not normally occur together.

**Recombinant Proteins:** Proteins created by recombinant DNA technology.

**Regenerative Medicine:** Research into treatments that restore damaged cells with healthy, disease-free cells.

**Restriction Enzymes:** Enzymes having the ability to cut DNA at a certain location. Scientists use these enzymes to isolate certain types of DNA and place them into new environments. Where DNA ligase is the glue of recombinant DNA technology, restriction enzymes are the scissors.

**Reverse Transcriptase:** An enzyme used by retroviruses to form a complementary DNA sequence (cDNA) from an RNA template—usually the genome of the retrovirus. The enzyme then performs a complementary template of the cDNA strand such that a double-stranded DNA molecule is formed. This double-stranded DNA molecule is then inserted into the chromosome

of the host cell, which has been infected by the retrovirus.

**Ribonucleic Acid (RNA):** A molecule similar to DNA, which helps in the process of decoding the genetic information carried by DNA. RNA is a nucleic acid transcribed from DNA; mRNA is then translated into proteins.

**Ribosome:** The cell structures within which protein synthesis occurs.

**RNA Interference:** A mechanism that inhibits gene expression at the stage of translation (see **translation**) or by hindering the transcription (see **transcription**) of specific genes. This method has been referred to as posttranscriptional gene silencing and is an important tool for gene-expression research.

**Signal Transduction:** The movement of signals from the outside of a cell to the inside. Scientists are attempting to learn more about this process in cancer cells in order to fight the disease.

**Single-Nucleotide Polymorphism (SNP):** A DNA sequence variation that occurs when a single nucleotide—A, T, G or C—in the genome differs between members of a species. Variations in the DNA sequences of humans can affect how humans develop diseases and respond to pathogens, chemicals, drugs, vaccines and other agents.

**Southern Blotting:** Transfer by absorption of DNA fragments separated in electrophoretic gels to membrane filters for detection of specific base sequences by radiolabeled complementary probes.

**Stem Cell:** Undifferentiated, human cells with the ability both to multiply and to differentiate into specific cells.

**Thermocycler:** A laboratory apparatus, used to amplify segments of DNA via the polymerase chain reaction (PCR) process. The device has a thermal block with holes where tubes holding the PCR mixtures can be inserted. The cyler then raises and lowers the temperature of the block in discrete, preprogrammed steps.

**Transcription:** The process by which enzymes use the genetic information on a strand of DNA to create a complementary strand of messenger RNA.

**Transfer RNA:** Molecules that carry amino acids during the process of protein synthesis during translation.

**Transformation:** The process of transferring DNA from a donor to a recipient cell. Scientists use this process to introduce recombinant DNA to bacteria, yeast and mammalian cell lines.

**Transgenic:** A term describing an organism containing genetic material from a source other than its parents.

**Translation:** The process that converts an mRNA sequence into a string of amino acids that form a protein. Translation follows transcription (see **transcription**).

**Upstream Phase:** Involves the production of the protein product, most often by using cells (microbial, insect or mammalian) growing in culture.

**Vaccine:** An agent bearing antigens on its surface that causes activation of the immune system without causing actual disease.

**Vector:** (1) An organism that serves to transfer a disease-causing organism (pathogen) from one organism to another. (2) A mechanism whereby foreign genes are moved into an organism and inserted into that organism's genome.

**X-ray Crystallography:** A method of determining the arrangement of atoms within a crystal, in which a beam of X-rays strikes a crystal and scatters in many different directions. From the angles and intensities of these scattered beams, a crystallographer can produce a three-dimensional picture of the density of electrons within the crystal, and the structure of a substance can be determined.