GLOSSARY

Acetaldehyde: A toxic byproduct of alcohol *metabolism*.

Acetate: A compound produced from the *metabolism* of *acetaldehyde.*

Adduct: Product of the addition of one compound (e.g., *acetaldehyde)* to another compound (e.g., DNA).

Adenoma: A usually benign tumor of tissue lining the internal and external organs of the body (i.e., epithelial tissue) in which the tumor cells are arranged in a gland-like structure.

Adenomatous polyps: A tissue mass that bulges outward from the normal surface and which consists of benign tumor tissue; found, for example, in the colon.

Adenosine triphosphate (ATP): A molecule, generated largely in the *mitochondria*, that provides the energy needed for many key *metabolic* reactions.

Affinity: Measure of the strength with which an *enzyme* (e.g., *alcohol dehydrogenase [ADH]*) interacts with its target molecule (e.g., ethanol); an *enzyme* variant with a higher affinity can interact with its target at lower concentrations of the target molecule than an *enzyme* variant with a lower affinity.

Alcohol dehydrogenase (ADH): An *enzyme* that breaks down alcohol by *oxidation*, converting it to *acetaldehyde.* (See *cytochrome P450.)*

Aldehyde dehydrogenase (ALDH): An *enzyme* that converts *acetaldehyde* to *acetate.*

Allele: One of two or more variants of a certain gene.

Amine: A type of organic compound that contains nitrogen as a central atom.

Amino acids: The principal building blocks of *proteins* and *enzymes*.

Amino group: A group of atoms found in all *amines* and *amino acids.*

Antibody: A *protein* produced by certain immune cells that recognizes and binds to foreign *proteins,* leading to the destruction of those proteins.

Antibody-dependent cell-mediated cytotoxicity (ADCC): A mechanism of cell-mediated immunity whereby certain immune cells actively break up a target cell that has been bound by specific *antibodies*.

Antioxidant: A substance, such as glutathione, vitamin E, or an *enzyme*, that inhibits *oxidation* and that scavenges *free radicals* and protects the cell against damage caused by these radicals.

Apoptosis: Cell death in which the affected cell participates by activating a cascade of biochemical reactions that lead to death; also known as programmed cell death or cell suicide.

Aromatic amino acids: A class of *amino acids*, including phenylalanine and tryptophan, in which some of the constituent atoms form a ring.

Carcinogenesis: The process of initiating and promoting cancer.

Carcinoma: A malignant tumor of the epithelial tissue that tends to invade surrounding tissue and metastasize to other regions of the body.

Case–control study: An epidemiologic approach in which previously existing cases of a condition (e.g., a type of cancer) are compared with a control group of people who have similar characteristics (e.g., gender, age, and alcohol use history) but have not developed the condition under investigation; the two groups are compared to determine which factor (e.g., ALD allele) may account for the increased disease incidence in the case group.

Catalase: An *enzyme* that catalyzes the decomposition of hydrogen peroxide into water and oxygen.

Central vein: Blood vessel located in the center of each liver *lobule* through which cleansed blood exits the lobule and which feeds into the *hepatic vein;* also called hepatic venule.

Coenzyme: A nonprotein substance that combines with an *enzyme* to form a complete, functional complex.

Cohort study: An epidemiologic approach in which a group of people who share a common characteristic (e.g., who were all born in the same town or who all entered the an alcoholism treatment program) are fol-

lowed to determine which of them develop a certain condition (e.g., cancer).

Cytochrome P450: A family of *cytochromes*, one of which (CYP2E1) can oxidize alcohol to form *acetaldehyde*; high alcohol levels stimulate CYP2E1 activity.

Cytochromes: Specialized *enzymes* within *mitochondria* and other cell structures. Different cytochromes play important roles in metabolizing toxic substances, drugs, and other chemicals, as well as in producing *adenosine triphosphate (ATP)*.

Cytokines: A family of molecules, produced primarily by cells of the immune system, that regulate cellular interactions and other functions. Many cytokines play important roles in initiating and regulating inflammation.

Cytoplasm: The substance filling the cell, including the *cytosol* as well as *mitochondria*, *endoplasmic reticulum*, and other cell structures (organelles) but excluding the nucleus.

Cytosol: The fluid portion of the *cytoplasm*.

Dimer: Compound formed by the combination of two simpler molecules (subunits) that normally are not functional by themselves.

Electron: A subatomic particle with a negative charge.

Endocytosis: Mechanism by which specific molecules are ingested into the cell.

Endoplasmic reticulum: A system of folded membranes that loop back and forth, spreading throughout the *cytoplasm* and providing a large surface area for cell reactions.

Endothelial cells: Type of cell lining the body cavities and blood vessels; control the passage of materials and the transit of white blood cells into and out of the bloodstream.

Enzyme: A substance, usually a *protein*, that directs and accelerates chemical reactions in the body but does not itself undergo permanent change.

Ester: A compound formed from an acid and an alcohol.

Exon: Part of a gene that encodes a section of the mature *messenger RNA (mRNA)* by splicing and therefore is converted into a protein.

Expression (i.e., gene expression): The process by which the genetic information encoded in a gene's DNA sequence is converted into a functional *protein.*

Fatty acids: A major component of fats that is used by the body for energy and tissue development.

Fibrosis: The formation of scar tissue.

Free radicals: Highly reactive molecular fragments that frequently contain oxygen. (See *reactive oxygen species [ROS].*)

Genotype: The complete genetic makeup of an organism determined by the particular combination of *alleles* for all genes.

Haplotype: Set of variations (e.g, s*ingle-nucleotide polymorphisms [SNPs]*) that are inherited together.

Hepatic vein: A large vessel that receives blood after it has passed through the *central veins* of the liver *lobules*.

Hepatocytes: The principal cells of the liver, which carry out most of the liver's metabolic activities.

Heterodimer: *Dimer* made up of two different subunits.

Heterozygous: Carrying two different *alleles* of a given gene.

Homodimer: *Dimer* made up of two identical subunits.

Homozygous: Carrying two copies of the same *allele* of a given gene.

Hyperlipidemia: Excess fat in the blood.

Hyperuricemia: Excess uric acid in the blood.

Hypoxia: Lower-than-normal levels of oxygen.

In vitro: Latin term meaning "in glass"; refers to experiments that are not conducted in an intact organism but in a test tube.

Intron: DNA sequence located between two *exons* in a gene; although it is *transcribed* during gene expression, it is removed from the final *messenger RNA (mRNA)* by splicing and therefore is not converted into *protein*.

Isozymes/Isoenzymes: *Enzymes* that differ in *amino acid* sequence but catalyze the same chemical reaction.

Ketosis: Abnormal accumulation in the body of ketones, which are end products of fatty acid *metabolism.* Ketosis occurs when the body cannot metabolize sufficient carbohydrates to generate the energy needed (e.g., in patients with diabetes or during starvation).

Kinetic properties: Variables that describe the activity of an *enzyme*, such as its turnover rate (i.e., the number of reactions it can perform during 1 minute) or its binding constant (K_m), which describes the *enzyme's affinity* to its target molecule.

K_m: A measurement used to describe the activity of an *enzyme*. It describes the concentration of the *enzyme's substrate* at which the *enzyme* works at 50 percent capacity.

Kupffer cells: Specialized immune cells in the liver that filter bacteria and other foreign substances from the blood and produce *antibodies* and *cytokines*. (See also *sinusoids*.)

Lactic acidosis: A condition characterized by the accumulation of lactic acid in bodily tissues.

Linkage disequilibrium (LD): Phenomenon in which *alleles* at two or more sites on a chromosome are not randomly associated—that is, a particular *allele* at one site may almost always occur on chromosomes with a specific *allele* at another site. For example, there are two coding *single-nucleotide polymorphisms (SNPs)* in *ADH1C,* but instead of all four possible combinations of the two *amino acids* (as would be expected if the *SNPs* were randomly associated), only two forms are commonly found.

Linkage study: The comparison of two groups of subjects (e.g., people with and without a given disease) to evaluate association between an *allele* and a *phenotype* (e.g., a disease).

Lipids: Fatty substances, including simple fats, their major components (i.e., *fatty acids*), and various fat-soluble substances (e.g., cholesterol).

Lipid peroxidation: The sequential breakdown of fatty substances in cells by chemical *oxidation*, leading eventually to the destruction of membranes within and surrounding the cell.

Lobule: A cylindrical structure about 2 millimeters in diameter that is the basic functional unit of the liver. The liver can be composed of up to 100,000 lobules.

Macrophage: A type of immune cell that ingests foreign particles and microorganisms and synthesizes *proteins* and other substances important in inflammatory responses, including *cytokines*. Macrophages that reside in the liver are called *Kupffer cells*.

messenger RNA (mRNA): Intermediary molecule generated during the process of converting the genetic information encoded in the DNA into *protein* products.

Metabolism: The totality of chemical reactions occurring in a cell, an organ, or the body. The term sometimes is applied more narrowly to the breakdown of a particular substance (e.g., alcohol) by specific *enzymes*.

Microsomes: Small *vesicles* derived from fragmented *endoplasmic reticulum* produced when tissues such as liver are mechanically broken (homogenized). Microsomes contain the cell's *cytochrome P450 (CYP) enzymes,* involved in *oxidative metabolism*.

Microsomal ethanol-oxidizing system: An *enzyme* system involving *cytochrome P450* that breaks down alcohol and generates toxic products, such as *acetaldehyde* and *reactive oxygen species (ROS)*.

Microtubules: Any of the minute tubules in cell *cytoplasm* that are composed of the *protein* tubulin and form important structural components.

Mitochondria: Structures within cells that generate most of the cells' energy through the production of *adenosine triphosphate (ATP)*.

Mitochondrial electron transport system: see *Respiratory chain.*

Morphologic: Pertaining to the physical shape and size of an organ, tissue, or cell.

Mucosa: Mucous membrane; a thin sheet of tissue that lines cavities or canals of the body that open to the

outside (e.g., the aerodigestive tract) and which, among other functions, secretes mucus.

Mutagenic: Causing a genetic *mutation* or increase in *mutation* rate.

Mutation: A change in the genetic material that can occur either spontaneously or can be induced by a chemical or other process.

Nicotinamide adenine dinucleotide (NAD^+): NAD is a molecule that can bind with hydrogen atoms and become reduced NAD, or NADH; it acts as a *coenyzme* that interacts with numerous *enyzmes* (including *alcohol dehydrogenase [ADH]*). NAD and NADH serve as a hydrogen acceptor and donor, respectively, during enzymatic reactions, thereby helping to maintain balance between *oxidation* and *reduction* in the cell.

Nucleotide: Building block of DNA and other related molecules.

Odds ratio: The ratio of the odds of an event (e.g., development of alcoholism) occurring in one group of individuals (e.g., people with the *ALDH2*2 allele*) versus the odds of that event occurring in another group (e.g., people with the *ALDH2*1 allele*); an odds ratio <1.0 indicates that the first group has a reduced risk of the event, whereas an odds ratio >1 indicates that the first group has an increased risk of the event compared with the second group.

Oncogene: A potentially cancer-inducing gene that under normal conditions plays a role in growth and proliferation of cells but which, when activated in some way, may cause the cell to multiply uncontrollably.

Oxidation: A chemical reaction that results in a loss of electrons by a substance and which usually involves removing a hydrogen atom from a molecule or adding oxygen to it, or both. (See *reduction*.)

Oxidative stress: An imbalance between oxidants (e.g., *free radicals*) and *antioxidants* that can lead to excessive *oxidation* and cell damage.

Pancreatitis: An acute or chronic inflammation of the pancreas.

Perivenous: Referring to the region of a liver *lobule* surrounding the *central vein*.

Peroxisomes: A cytoplasmic cell organelle containing *enzymes* that act in the production and decomposition of hydrogen peroxide.

Phospholipid: A *lipid* that contains a phosphate group.

Polyamine: Any compound that contains two or more amine (NH_2) chemical groups; many polyamines occur naturally in the tissues, particularly in rapidly growing tissues.

Polymorphism: Existence of a gene in several *allelic* forms.

Proliferation: The growth and reproduction of cells.

Promoter: Set of DNA elements that regulate in which cell, at what time, and in what amount a gene is expressed and which specifies the *transcription* start site.

Proteins: Molecules composed of chains of *amino acids* linked together. Proteins help maintain the cell's structure and participate in many biological functions, including the regulation of metabolic reactions. The shape and function of a protein is determined by the sequence of its *amino acids*.

Reactive oxygen species (ROS): Highly reactive oxygen-containing *free radicals* that are generated during *oxidative metabolism*. ROS can react with and damage *lipids, proteins,* and DNA in cells, causing *oxidative stress*. Common ROS include hydrogen peroxide, *superoxide* radicals, and hydroxyl radicals.

Receptor: A *protein* on the surface of a cell that recognizes and binds to chemical messengers.

Recombination: Rearrangement of genetic material during the production of the germ cells that results in a unique combination of genes in each individual; appears more commonly to occur at certain sites on the DNA (hot spots) than would be expected by chance alone.

Redox/Redox state: Shorthand for *reduction/oxidation* reactions. The term redox state is often used to describe the balance of *NAD^+* and *NADH* in a biological system such as a cell or organ. An abnormal redox state can develop in a variety of deleterious situations.

Reduction: The reverse of *oxidation*, reduction is a chemical reaction that results in a gain of *electrons* by a sub-

stance and which usually involves removing an oxygen atom from a molecule, or adding hydrogen to it, or both.

Relative risk: The ratio of the frequency of a certain disorders (e.g., cancer) in groups exposed to a certain risk factor (e.g., heavy alcohol consumption) and in groups not exposed to the risk factor.

Respiratory chain: The *electron* transport system located in the *mitochondria*, in which *electrons* released by *NADH* are passed on to a series of other molecules that first accept the *electrons* and then pass them on to the next molecule in the chain. The *electrons* ultimately are transferred to oxygen to generate water. These successive reactions provide enough energy to drive the synthesis of *adenosine triphosphate* (*ATP)* molecules.

Retinol: Vitamin A.

Salivary gland: One of three pairs of glands located around the mouth that secrete saliva into the mouth.

Single-nucleotide polymorphism (SNP): Genetic variation that results from the exchange of only a single *nucleotide*.

Sinusoids: Channels in a liver *lobule* that bring blood and nutrients to the *hepatocytes*, similar to capillaries in other organs. Sinusoids are lined with *endothelial cells* and *Kupffer cells*.

Stellate cell: A star-shaped liver cell that serves as the primary storage site for vitamin A compounds and fat molecules; activation of stellate cells plays a central role in the development of *fibrosis*.

Substrate: A substance upon which an *enzyme* acts.

Superoxide: A destructive *reactive oxygen species (ROS)* produced as a byproduct of some *oxidation* reactions.

Synergistic effects: The combined effect of two factors or drugs that is greater than the sum of the effects of both factors individually.

Transcription: Process by which the genetic information contained in the genes on the DNA is copied into an intermediary molecule (*messenger RNA [mRNA]*) that then serves as the template for *translation*.

Translation: Process during which a *protein* is generated from *amino acids* based on the information carried in the *messenger RNA (mRNA)*.

Tumor necrosis factor alpha (TNF-α): A type of *cytokine* that promotes inflammatory responses, stimulates neutrophils and *macrophages,* induces fever, and induces *macrophages* to produce *cytokines*.

Tumor suppressor gene: A gene whose product normally serves to control cell growth and which, when inactivated, may cause the cell to multiply uncontrollably (also see *oncogene*).