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Glossary of Acronyms and Terms

Glossary of Acronyms

A —Adenine
AEC —Atomic Energy Commission
ATSDR —Agency for Toxic Substances and Disease Registry (Centers for Disease Control)
BEIR –Committee on the Biological Effects of Ionizing Radiations (NRC)
C —Cytosine
CERCLA —Comprehensive Environmental Response, Compensation, and Liability Act ("Superfund")
DNA —Deoxyribonucleic Acid
DOE —Department of Energy
EBV —Epstein-Barr Virus
EDB —Ethylene dibromide
EPA —Environmental Protection Agency
ENU —Ethylnitrosourea
EtO —Ethylene oxide
FDA –Food and Drug Administration (DHHS)
FRC —Federal Radiation Council
G —Guanine
HbA —Hemoglobin A
HbM —Hemoglobin M
hprt —Hypoxanthineguanine phosphoribosyl transferase (gene)
HPRT —Hypoxanthineguanine phosphoribosyl transferase (enzyme)
HTT —Heritable Translocation Test
ICPEMC —International Commission for Protection Against Environmental Mutagens and Carcinogens
ICRP —International Commission on Radiological Protection
mRNA –Messenger RNA
MSHA —Mine Safety and Health Administration (Department of Labor)
NCRP —National Council on Radiation Protection and Measurements
NIH —National Institutes of Health
NRC —Nuclear Regulatory Commission
NRC —National Research Council (National Academy of Sciences)
NTP –National Toxicology Program (DHHS)
OSHA –Occupational Safety and Health Administration (Department of Labor)
OTA –Office of Technology Assessment (U.S. Congress)
PBL –Peripheral Blood Lymphocyte
PFGE —Pulsed Field Gel Electrophoresis
PKU —Phenylketonuria
R —Roentgen
RFLP —Restriction Fragment Length Polymorphism
RNA —Ribonucleic Acid
SCE —Sister-chromatid Exchange
SLT —Specific Locus Test
T —Thymine
TG^r —Thioguanine resistant
TSCA —Toxic Substances Control Act
UNSCEAR—United Nations Scientific Committee on the Effects of Atomic Radiation
2DDGGE —Two Dimensional Denaturing Gel Electrophoresis
2DPAGE —Two Dimensional Polyacrylamide Gel Electrophoresis
6TG —6Thioguanine
$6TG^r$ —6Thioguanine resistant

Glossary of Terms

Achondroplasia: A disease marked by a defect in the formation of cartilage at the ends of long bones (femur, humerus) that leads to a type of dwarfism. There are a number of hereditary forms, the most common of which is autosomal dominant.

Allele: An alternative form of a gene, or a group of functionally related genes, located at the corresponding site on a homologous chromosome. Each allele is inherited separately from each parent. Alleles can be dominant, recessive, or co-dominant for a particular trait.

Alpha thalassemia: A genetic defect caused by an alteration in a portion of the gene coding for the alpha globin molecule. The result is an insufficient number of alpha globin molecules and a deficiency of adult hemoglobin.

Amino acid: One of a group of *20* molecules that bind together in various sequences to form all protein molecules. The specific sequence of amino acids determines the structure and function of a protein.

Amniocentesis: A procedure that involves withdrawing a sample (usually *2* to *8* milliliters) of the amniotic fluid surrounding the fetus in utero. This fluid contains cells shed by the developing fetus. The cells can be grown in cell culture and analyzed either biochemically or cytogenetically to detect a variety of genetic abnormalities in the fetus, including genetic diseases such as Down syndrome and Tay Sachs disease.

Autoradiography: A technique for identifying radioactively-labeled molecules or fragments of molecules, useful for analyzing DNA for the presence of mutations.

Autosome: A chromosome not involved in sex-determination. In a complete set of human chromosomes, there are 44 autosomes (22 pairs of homologous chromosomes) and a pair of sex-determining chromosomes.

Base pair (of nucleic adds): A pair of hydrogen-bonded nitrogenous bases (one purine and one pyrimidine) that join the two strands of the DNA double helix. Adenine pairs with thymine, and cytosine pairs with guanine.

Beta globin: A constituent of hemoglobin, which is a molecule consisting of four globin subunits and a heme group (two alpha and two beta globins).

Carcinogen: A chemical or physical agent that causes cancer.

Cell: The smallest membrane-bound protoplasmic body, consisting of a nucleus and its surrounding cytoplasm, capable of independent reproduction.

Cell culture: Growth in the laboratory of cells isolated from multicellular organisms. Each culture is usually of one cell type (e.g., lymphocytes, fibroblasts, etc.).

Cell line: A sample of cells, having undergone the process of adaptation to artificial laboratory cultivation, that is now capable of sustaining continuous, long-term growth in culture.

Chromosome: A threadlike structure that carries genetic information arranged in a linear sequence. It consists of a complex of nucleic acids and proteins.

Chromosome abnormalities: A group of pathological conditions associated with abnormalities in the number or structure (e.g., insertions, deletions, rearrangements) of chromosomes.

Chromosome banding: The chemical process of staining chromosomes to identify each pair of homologous chromosomes. Staining by various techniques produces patterns of light and dark bands (visible under the microscope) that are characteristic of each chromosome pair. Chromosome banding is particularly useful in detecting structural chromosome abnormalities such as inversions and deletions.

Codon: A sequence of 3 adjacent nucleotides in mRNA that specifies 1 of the 20 amino acids or the initiation or termination of the peptide chain. The linear sequence of codons determines the order in which amino acids are added to a polypeptide chain during translation.

Complementary DNA (cDNA): Single-stranded DNA that is synthesized from a messenger RNA template. It is often used as a probe to help locate a specific gene in an organism.

Congenital: Refers to a condition that is present at birth.

Congenital abnormality: Any abnormality, genetic or nongenetic, that is present at birth.

Cytoplasm: The contents of a cell exclusive of the nucleus. It consists of an aqueous solution and the organelles suspended in it and is the site of most chemical activities of the cell, including protein synthesis.

Denaturation: The separation of double-stranded DNA into its complementary, separate strands by treatment with chemicals or heat. The narrow range of temperature or chemical concentration at which DNA denaturation occurs is characteristic of the nucleotide sequence of the particular molecule.

Diploid: The chromosome state in which each homologous chromosome is present in pairs. All human somatic cells are diploid (i.e., they have *46* chromosomes), whereas reproductive cells, with 23 chromosomes, are haploid.

DNA: Deoxyribonucleic acid. The nucleic acid in chromosomes that contains the genetic information. The molecule is double-stranded, with an external "backbone" formed by a chain of alternating phosphate and sugar (deoxyribose) units and an internal ladder-like structure formed by nucleotide base-pairs held together by hydrogen bonds. The nucleotide base pairs consist of the bases adenine (A), cytosine (C), guanine (G), and thymine (T), whose structures are such that A can hydrogen bond with T, and C with G. The sequence of each individual strand can be deduced by knowing that of its partner. This complementarily is the key to the information-transmitting capabilities of DNA. (See also nucleotide and gene.)

DNA probe: A segment of complementary DNA that is used to detect the presence of a particular nucleotide base sequence.

DNA sequence: The order of nucleotide bases in DNA.

Dominant: A term used to refer to a genetic trait that is expressed in an individual who is heterozygous for a particular gene. Compare recessive.

Down syndrome: A genetic abnormality characterized by mental retardation, congenital heart defects, immune system abnormalities, various morphological abnormalities and a reduced life expectancy. Down syndrome is caused by either an extra copy of chromosome 21 (called trisomy 21) or by two copies of chromosome 21 and another chromosome 21 translocated to a different chromosome (usually to chromosome *14).* The latter results in "translocation Down syndrome." Trisomy 21 has been shown to increase in frequency with advanced maternal age.

Electrophoresis: A technique used to separate molecules (such as DNA fragments or proteins) from a mixture of similar molecules. By passing an electric current through a medium containing the mixture, each type of molecule travels through the medium at a rate that corresponds to its electric charge and size. Separation is based on differences in net electrical charge and in size or arrangement of the molecule.

Enzyme: A protein that catalyzes a chemical reaction without being permanentl, altered or consumed by the reaction, so that it can be used repeatedly.

Enzyme deficiency variants: Abnormal proteins characterized by reduction or elimination of enzymatic activity. These changes may be caused by the absence of a gene product, or the presence of proteins that are non-functional or abnormally unstable.

Epidemiologic studies: Studies concerned with the relationships of various factors determining the frequency and distribution of diseases in a human population.

Escherichia coli (E. coli): A species of rod-shaped, gram negative bacteria that inhabit the normal intestinal tract of vertebrates. Many nonpathogenic strains of E. coli are hosts in recombinant DNA technologies.

Eukaryote: Cells or organisms with membrane-bound, structurally discrete nuclei and well-developed cell organelles. Eukaryotes include all organisms except viruses, bacteria, and blue-green algae. Compare *prokaryote.*

Exons: DNA sequences that determine the sequence of amino acids in proteins. Exons are separated on the DNA by introns, or intervening sequences, that are transcribed and later removed, or spliced out, during the production of mature messenger RNA.

Gametes: Mature male or female reproductive cells (germ cells: sperm or ova) with a haploid chromosome content *(23* chromosomes in humans).

Gene: A linear sequence of nucleotides in DNA that is needed to synthesize a protein and/or regulate cell functions. A mutation in one or more of the nucleotides in a gene may lead to abnormalities in the structure of the gene product or in the amount of gene product synthesized.

Genetic code: The sequence of nucleotide triplets along the DNA that determines the sequence of amino acids in protein synthesis. This code is common to nearly all living organisms.

Genome: A term used to refer to all the genetic material carried by a single gamete.

Genotype: The genetic constitution of an organism, as distinguished from its physical appearance (its phenotype). For example, an individual may have a heterozygous genotype for eye color consisting of an allele for brown eyes (which is dominant) and an allele for blue eyes (which is recessive) or a homozygous genotype, with two alleles (both dominant) for brown eyes. In either case, the phenotype is the same: brown eyes.

Germinal mutations: Mutations in the DNA of reproductive cells—egg or sperm. Germinal mutations can be transmitted to the offspring only if one of those particular germ cells is involved in fertilization.

Germ line: The tissue or cell line that produces gametes and is used for reproductive purposes, as opposed to tissue or cell line from somatic cells. Also known as "germinal tissue."

Haploid: Half of the full set of genetic material, or one chromosome of each homologous pair. Gametes have a haploid set of DNA. Fertilization of an ovum by a sperm produces a diploid number of chromosomes in the zygote.

Hemoglobin: The oxygen-carrying molecule found in red blood cells. Adult hemoglobin is a protein composed of a single heme group bound to two alpha globin chains and two beta globin chains.

Hemoglobinopathies: A collection of hereditary disorders of hemoglobin structure and/or function. Examples are thalassemia and sickle cell anemia.

Hemophilia: A genetic disorder distinguished by a deficiency of one or more coagulation factors—e.g., Factor VIII (hemophilia A) or Factor IX (hemophilia B). The underlying mutations are located on the X chromosome. Hemophilia occurs most often in males who have only one X chromosome, and is transmitted to offspring by asymptomatic females, who have two X chromosomes, one of which carries the hemophilia mutation.

Heritable mutation: A mutation that is passed from parent to offspring and was present in a germ cell of one of the parents.

Heteroduplex: A double-stranded nucleic acid molecule composed of individual strands of different origin, e.g., a parent's DNA strand hybridized to a child's DNA strand, or RNA hybridized to DNA.

Heterozygote: An individual who has two different alleles of any one particular gene, e.g., an individual who has one copy of the gene for thalassemia at the locus for beta globin is heterozygous for this trait.

Homoduplex: A double-stranded nucleic acid molecule composed of two strands of the same origin, e.g., genomic DNA isolated from human ceils (DNA hybridized with DNA from the same individual).

Homozygote: An individual with the same allele at both genes responsible for a particular trait.

Homozygous: Having identical alleles at a given locus. Compare *heterozygous*.

Hybridization: The process of joining two single-strands of RNA or DNA together so that they become a double-stranded molecule. For hybridization to occur, the two strands must be nearly or perfectly complementary in the sequence of the nucleotide base pairs.

Induced mutation: A change in the structure of DNA or the number of chromosomes, caused by exposure of the DNA to a mutagenic agent.

In vitro: Literally, "in glass," pertaining to a *biological* process or reaction taking place in an artificial environment, usually a laboratory. Sometimes used to include the growth of cells from multicellular organisms under cell culture conditions.

In vivo: Literally, "in the living," pertaining to a biological process or reaction taking place in a living cell or organism.

Karyotype: A photomicrograph of an individual's chromosomes arranged in a standard format, showing the number, size, and shape of each chromosome.

Kilobase: A unit of measurement for the length of nucleic acids along a chromosome. One kilobase (abbreviated kb) consists of 1,000 nucleotide bases. Genes can be several kilobases in length.

Lambda: A bacterial virus that infects E. coli, producing many copies of itself within the bacterium.

Lesch-Nyhan syndrome: An X-linked recessive disorder characterized by compulsive self-mutilation and other mental and behavioral abnormalities. It is caused by a defect in the gene that produces a particular enzyme (hypoxanthine-guanine phosphoribosyl transferase) important in metabolism. The causal relationship to the behavioral aspects of the disorder is not yet understood.

Locus: The position of a gene or of a group of functionally related genes on a chromosome.

Locus Test: A measurement of genes examined in a study of mutant proteins, based on the number of proteins examined, on the number of gene loci represented by each such protein, and on the number of individual samples obtained.

Lymphocytes: Specialized white blood cells involved in the body's immune response. B-lymphocytes originate in the bone marrow and when stimulated by an antigen produce circulating antibodies (humoral immunity). T-lymphocytes are produced in the bone marrow and mature in the thymus gland and engage in a type of defense that does not depend directly on antibody attack (cell-mediated immunity).

Marfan's syndrome: A genetic disorder characterized by abnormally long fingers and toes and by abnormalities of the eye lenses and heart. (Abraham Lincoln is thought by some to have suffered from this disease). Also called arachnodactyly ("spider fingeredness").

Meiosis: The process of cell division in reproductive cells that reduces the number of chromosomes to half of the full set so that each parent contributes half of the genetic material to each offspring. When the egg and sperm fuse at conception, the full set of chromosomes (a total of 46 chromosomes in humans) is restored in the offspring.

Mendelian: A term used to refer to a trait that follows Mendel's laws of inheritance and is controlled by a single gene, and which therefore shows a simple pattern of inheritance (dominant or recessive). So named because traits of this sort were first recognized by Gregor Mendel, the Austrian monk whose early research laid the basis for modern genetics. Mendel's laws include the Law of Segregation, which describes how each pair of alleles separates into different gametes and the Law of Independent Assortment, which describes how different alleles are assorted independently of the other alleles in gametes and how the subsequent pairing of male and female gametes occurs randomly.

Messenger RNA (mRNA): Ribonucleic acid that serves as the template for protein synthesis. It is produced by transcribing a DNA sequence into a complementary RNA sequence. Messenger RNA molecules carry the instructions for assembling proteins on the ribosomes.

Mitosis: The process of division involving DNA replication, and resulting in two daughter cells with the same number of chromosomes and cytoplasmic material as the parent cell.

Multifactorial traits: Traits that are not determined solely by a single gene. Multifactorial, or polygenic, traits (e.g., height) have variable phenotypic effects that depend for their expression on the interaction of many genes and environmental influences.

Mutagen: A chemical or physical agent that causes changes in the structure of DNA.

Mutation rate: The number of mutations per unit of DNA (e.g., per gene, per nucleotide, per genome, etc.) occurring per unit of time (usually per generation).

Mutations: Changes in the composition of DNA, generally divided according to size into "gene mutations" (changes within a single gene, such as nucleotide substitutions) and "chromosome mutations" (affecting larger portions of the chromosome, or the loss or addition of an entire chromosome). A "heritable mutation" is a mutation that is passed from parent to offspring and therefore was present in the germ cell of one of the parents. See also *induced mutation* and *spontaneous mutation.*

Nucleic acids: Macromolecules composed of sequences of nucleotides that carry genetic information, There are two kinds of nucleic acids: DNA, containing the sugar deoxyribose and RNA, containing the sugar ribose.

Nucleotide: A subunit of DNA or RNA, consisting of a nitrogenous base (adenine, guanine, thymine, cytosine, or uridine), a phosphate molecule, and a sugar molecule (deoxyribose in DNA or ribose in RNA). The linkage of thousands of these subunits forms the DNA or RNA molecule.

Nucleus: The intracellular structure of eukaryotes that contains DNA.

Oligonucleotide: A polymer made up of a few (generally fewer than 10 or 20) nucleotides; a short sequence of DNA or RNA.

Peptide: A compound consisting of two or more amino acids linked together, formed through a chemical process that produces one molecule of water for each joining of one amino acid to another. Peptides are the building blocks of proteins.

Phenotype: The appearance of an individual or the observable properties of an organism that result from the interaction of genes and the environment.

PhenyIketonuria (PKU): An autosomal recessive genetic disorder of amino acid metabolism, caused by the inability to metabolize phenylalanine to tyrosine. The resulting accumulation of phenylalanine and derived products causes mental retardation, which can be avoided by dietary restriction of phenylalanine beginning soon after birth.

Polymorphism: A single gene trait (e.g., a red blood cell surface antigen) that exists in two or more alternative forms (such as types A, B, AB, and O blood). Genetic variants are considered polymorphisms if their frequency exceeds 1 percent each, but are considered "rare mutations" if they are found in less than 1 percent of the population.

Polypeptide: A sequence of amino acids joined in a chain.

Probe: A molecule that has been tagged or labeled in some way with a tracer substance (a radioactive isotope or specific dye-absorbing compound) that is used to locate or identify a specific gene or gene product. For example, a radioactive mRNA probe for a DNA gene, or a monoclinal antibody probe for a specific protein. See also *DNA probes*.

Prokaryote: A cell or organism lacking membrane-bound, structurally discrete nuclei. Compare *eukaryote*.

Protein: A molecule composed of hundreds of linked amino acids in a specific sequence, which is, in turn, determined by the sequence of nucleotides in DNA. Proteins are required for the structure, function, and regulation of cells, tissues, and organs in the body.

Recessive: A genetic trait that is manifested phenotypically only when both alleles for the trait are present at a locus. E.g., sickle cell anemia is manifest only when both copies of the gene for beta globin contain the beta^{s} mutation, whereas when individuals have only one copy of the beta^{s} gene, they do not develop the disease, but have sickle-cell trait, a generally benign condition. X-linked traits act as if they were recessive in females and dominant in males. Compare *dominant*.

Recombinant DNA (rDNA) technology: Techniques involving the incorporation of DNA fragments, generated with the use of restriction enzymes, into a suitable host organism's DNA (a vector). The host is then grown in culture to produce clones with multiple copies of the incorporated DNA fragment. The clones containing this particular DNA fragment can then be selected and harvested.

Replication: The synthesis of new DNA from existing DNA.

Restriction enzyme: An enzyme that has the ability to recognize a specific nucleotide sequence in a nucleic acid (ranging from 4 to 12 base pairs in length) and cut or cleave the nucleic acid at that sequence. They are termed "restriction" enzymes because, occurrin$_{g}$ naturally in bacteria, they recognize foreign nucleic acid (e. g., the DNA of a bacterial virus as it begins to infect and destroy its host) and destroy it, thus restricting the ability of the virus to prey upon certain potential host strains. Over 400 different restriction *enzymes* are known, recognizing a great variety of different nucleotide base sequences. Use of restriction enzymes has made possible the cutting and splicing together of nucleic acid within and between different organisms and species.

Restriction Fragment Length Polymorphism (RFLP): Fragments of DNA that may vary in length from individual to individual, depending on the presence of polymorphisms or rare mutations.

Ribosome: A cellular organelle that is the site of protein synthesis, the process of reading the instructions in mRNA and using it as the guide to constructing the specified protein.

RNA (ribonucleic acid): The nucleic acid found mainly in the nucleus and ribosomes and is involved in the control of cellular activities. There are several classes of RNA that serve different purposes, including messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). The functions of various kinds of RNA include "translating" selected gene sequences coded in the cell's DNA, and transferring that information outside of the nucleus to structures that then synthesize the proteins indicated by the RNA vehicle.

RNaseA: An enzyme that cleaves RNA where certain sequences of nucleotide bases occur. RNaseA has been used to cut fragments of RNA/DNA heteroduplexes where particular mismatches in the heteroduplexes occur.

Sentinel phenotypes: A group of autosomal dominant or X-linked conditions that can occur sporadically. They are thought to result from new germinal mutations in the parents' reproductive cells.

Sex chromosomes: The X and the Y chromosomes, 2 of the *46* chromosomes in human cells, that determine the sex of the individual. Females have two X chromosomes, while males have one X and one Y chromosome.

Sickle-cell disease: A genetic disorder of hemoglobin function caused by the presence of an abnormal beta globin chain. Patients with sickle-cell disease have red blood cells that tend to deform into a sickle-like shape. The specific defect is caused by an abnormal gene, resulting in the replacement of the usual amino acid, glutamic acid, with valine, in the sixth amino acid position in the beta-hemoglobin molecule. This increases its propensity to crystallize, thus rupturing the red blood cell and causing the cells to lodge in small blood vessels. Also called "sickle-cell anemia." See sickle-cezl trait.

Sickle-cell trait: The generally benign condition shown

by individuals carrying the variant beta^{s} gene as well as the normal beta^{a} gene. Such individuals are heterozygous for the sickle-cell gene, and are healthy (i.e., are usually asymptomatic), but two heterozygous parents have a *25* percent risk with each pregnancy of having a child with *homozygous* sickle-cell disease.

Single gene disorder: A genetic disease caused by a single gene and showing a simple pattern of inheritance (e.g., dominant or recessive, autosomal or X-Iinked). Also called "Mendelian disorder."

Somatic: A term used to refer to body tissues, as opposed to reproductive (germinal) tissues.

Somatic cell: Any cell in the body except reproductive cells or their precursors.

Spontaneous mutation: In the absence of any known causative agent, a change in the structure of DNA or in the number of chromosomes. Also called a "background" mutation. Also see *mutations*.

Stem cells: Undifferentiated cells in the bone marrow that have the ability to replicate and to differentiate into blood cells.

Tay-Sachs disease: An autosomal recessive genetic disease resulting in developmental retardation, paralysis, dementia and blindness, usually fatal in early childhood. The defective gene codes for hexosaminidase A, an enzyme that is involved in certain chemical pathways in the brain. Symptoms are caused by an accumulation of cerebral gangliosides, fatty acid and sugar molecules found in the brain and nervous tissue. The gene is found in highest frequency among Jews of Eastern European origin.

Teratogen: A physical or chemical agent (e.g., thalidomide, radiation, alcohol, etc.) that can cause congenital abnormalities as a result of exposure in utero.

Tetramer: A complex molecule consisting of four major portions joined together (e.g., hemoglobin, in which two alpha chains and two beta chains are joined to a central heme group.)

Thalassemia: A group of autosomal recessive genetic disorders characterized by abnormalities in synthesis of the globin polypeptides of hemoglobin. The two most common forms are alpha-thalassemia and beta-thalassemia, disorders of the alpha- and beta-globin polypeptides, respectively, which cause imbalances in the production of the globins and lead to an overall deficiency of adult hemoglobin. The thalassemias are most common in people of Mediterranean, Middle Eastern, and Asian descent.

T-lymphocytes: See *Lymphocytes,*

Transcription: The synthesis of messenger RNA (mRNA) on a DNA template. The resulting RNA sequence is complementary to the DNA sequence.

Transfer RNA (tRNA): Specialized RNA molecules that function to bring specific amino acids to ribosomes that translate messenger RNA (mRNA) into proteins.

Translation: The process in which the genetic code contained in the nucleotide base sequence of messenger RNA directs the synthesis of a specific order of amino acids to produce a protein.

Trisomy: The presence of an extra chromosome, resulting in three homologous chromosomes instead of two, e.g., Down syndrome can result from Trisomy 21, or the presence of an extra chromosome number 21 in each body cell.

tRNA: See *transfer RNA.*

X-linked mutation: A mutation that occurs in a region of the X-chromosome.

Zygote: A fertilized egg that results from the fusion of sperm and egg.