# Basic Terminology

**Genetics:** The study of genes and their roles in inheritance

**Genetic testing:** Examines changes in an individual gene and/or set of genes that may account for the likelihood of a particular disease process

**Genomics:** The study of the complete set of a person's DNA/genes. Genomics also examines how genes interact with each other and how, or if, they are affected by environmental factors.

**Genomic testing:** Assesses an individual's genome (all of a person's genes, rather than a specific gene or set of genes)

**Diploid:** Containing two complete sets of chromosomes, one from each parent

**Genome:** 6 billion base pairs of DNA distributed unequally across 46 chromosomes (23 pairs) in a diploid genome

**Exome:** Part of the genome that includes just the DNA exons (about 1.5% of DNA in humans)

**Exons:** Sequences of DNA that encode proteins

**Transcriptome:** Gene expression profile; all the mRNAs transcribed from the genes of a cell at a given time

**Epigenetics:** Modifications in gene expression due to environmental factors and/or behaviors that effect how proteins and cells function but not changes in DNA sequences

**Somatic DNA:** DNA in cells that are not involved in reproduction and have a full complement of chromosomes (23 pairs in humans)

**Germline DNA:** DNA in cells involved in reproduction (ie, sperm and eggs) that have half as many chromosomes as somatic cells (23 individual chromosomes in humans)

**Germline susceptibility:** Genes a person is born with that may confer increased risk of disease

# Biomarkers

**Biomarker:** A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called "molecular marker" and "signature molecule."

**Biomarker testing:** As applied to genomics, analysis of single or multiple somatic genetic events associated with disease outcome including response to therapy; could be at DNA, RNA, or molecular level

**Diagnostic biomarker:** Associated with the diagnosis of a particular disease

**Prognostic biomarker:** Associated with the overall disease outcome regardless of treatment

**Predictive biomarker:** Associated with either a favorable or unfavorable outcome from a particular treatment

**Actionable biomarker:** Used to make treatment decisions

**Single nucleotide variant (SNV):** Any difference in a single DNA base pair irrespective of how often it occurs

**Single nucleotide polymorphism (SNP):** A single base pair difference considered normal common genetic variation

# DNA Alterations at the Chromosomal Level

**Cytogenetics:** Chromosomes in cells arrested in metaphase are stained through Giemsa banding; shows large gains, losses, and/or translocations of the entire chromosome complement

**Karyotype:** Image of normal human chromosomes lined up in pairs (include image)

**Inversions:** A portion of a chromosome which has broken off, turned upside down, and reattached

**Trisomy:** The presence of a third copy of a particular chromosome

**Monosomy:** The absence of one copy of a particular chromosome

**Insertions or deletions:** Changes the number of DNA bases in a gene by adding or removing a piece of DNA

**Amplification:** Small or large parts of chromosomes which have been duplicated or multiplied

**Translocations:** A piece of one chromosome which has broken off and attached to another chromosome

# Variations/Mutations

**Variation/mutation:** A change in the DNA sequence

**Point mutation:** A change within a gene in which one base pair in the original DNA sequence is altered

**Missense mutation:** A point mutation (usually) that results in a change in amino acid

**Deletion/insertion/duplication:** A few bases may be deleted, inserted, or duplicated

**Triplet repeats:** Sequence of 3 nucleotides that is repeated multiple times in DNA. This is a mechanism of inherited genetic disease that often occurs with neurodegenerative diseases.

**Frameshift mutation:** Insertion or deletion of bases that results in a shift to the reading frame of the DNA resulting in changes in AAs and/or a premature stop codon

**Somatic (acquired) mutations:** Occur after conception, during a person's life, and are only present in certain cells

**Germline (hereditary) mutations:** Inherited from a parent. They occur before conception and are present throughout a person's life in almost every cell in the body.

# Pathologic Variants

**Activating mutations:** Turns on the function of a gene that may normally be carefully regulated

**Fusions:** Portions of DNA that are attached to each other that should not be

**Clonal mutations:** In every cell of the cancer

**Subclonal mutations:** Only in a subset of cells of the cancer

**Driver mutations:** Thought to be key in promoting the initiation and/or survival of the cancer

**Passenger mutations:** Random mutations found within the cell that do not contribute directly to promoting the initiation and/or survival of the cancer; may be acquired prior to driver mutation

**Variant of undetermined significance (VUS):** A genetic change in the germline of unknown impact on the function of the gene

**Pathogenic mutations:** Directly contributes to disease development

# Pathologic Variants (cont.)

**Actionable mutations:** There is a specific therapy indicated

**Clonal hematopoiesis of indeterminate potential (CHIP):** Somatic mutation that occurs with aging in the normal blood cells; associated with increased subsequent risk of blood cancer and cardiovascular disease

**T cell clonality:** V(d)J rearrangements; unique T cell receptor used to diagnose a T cell malignancy

**B cell clonality:** IGH Clonality; unique B cell receptor sequence for a given B cell cancer that can be used to determine measurable residual disease (MRD, see Testing for definition) or for prognostic purposes in CLL

# Testing

**FISH (fluorescent in situ hybridization):** Uses a fluorescent probe to detect very small gains, losses, or translocations within a cell; FISH testing is able to detect changes that are too small to be seen on basic cytogenetic tests

**Immunohistochemistry (IHC):** Uses an antibody that is tagged with a dye or fluorescence against a cellular protein to study over- or under-expression of certain proteins

**Flow cytometry:** Cells in suspension with fluorescent-tagged antibodies are passed through a laser beam that activates fluorescence when the antibody target is present; used to detect whether multiple proteins are co-expressed on the same cell and to determine cell phenotype, which in turn strongly contributes to determining the diagnosis

**Sequencing:** Laboratory tests that examine the exact order of the four bases of DNA

**Sanger sequencing:** Low throughput sequencing often used to characterize one gene at a time

**Next generation sequencing (NGS):** High throughput sequencing used to characterize many genes or an entire genome at once; higher volume and more rapid than traditional Sanger sequencing

**Single cell sequencing:** Sequencing of RNA or DNA at single cell resolution

**Cell-free sequencing (liquid biopsy):** Sequencing of DNA in plasma

**Polymerase chain reaction (PCR):** Specific DNA probes are used to amplify a sequence to detect the presence or absence of a sequence of DNA; can detect very small amounts of DNA

# Testing (cont.)

**Genome editing** (e.g., CRISPR/Cas9): Approach to modifying a gene of interest by introducing a specific mutation into the endogenous gene

**Precision medicine:** A form of medicine that uses information about a person's own genes or proteins to prevent, diagnose, or treat disease. In cancer, precision medicine uses specific information about a person's tumor to help make a diagnosis, plan treatment, determine treatment effectiveness, or make a prognosis.

**Measurable (previously minimal) residual disease (MRD):** Describes detection of low levels of cancer cells after therapy; can be used to test for specific mutations. Definition has changed to measurable because minimal is dependent on what is measurable given the current state of technology.