JNCCN
Journal of the National Comprehensive Cancer Network

Supplemental online content for:

How Do We Make Clinical Molecular Testing for Cancer Standard of Care for Pathology Departments?

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J Natl Compr Canc Netw 2016;14(6):787–792

eAppendix 1. Glossary of Terms

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Activating mutation: A substitution of one amino acid residue by another that confers a new or higher activity upon the protein.	***miRNA:*** Short regulatory forms of RNA that bind to their target RNA and suppress its translation or alter its stability.
Allele frequency: The frequency of an allele (variant of a gene) at a particular locus.	***Multiplex sequencing platforms:*** A type of sequencing assay that simultaneously interrogates multiple genes/regions.
cell-free DNA: DNA circulating freely in the blood.	***Next-generation sequencing:*** High-throughput parallel sequencing procedure.
Clonal heterogeneity: A phenomenon by which cells within the same tumor can show distinct genetic and phenotypic profiles, including cellular morphology, gene expression, metabolism, motility, proliferation, and metastatic potential.	***Nonsynonymous mutation:*** A nucleotide change that alters the amino acid sequence of a protein usually resulting in a biological change in the function of the protein product.
Copy number variation: Structural variations that manifest as deletions or duplications in the genome.	***Novel mutation:*** A newly discovered mutation.
Depth of coverage: The number of times a specific nucleotide is read during the sequencing process.	***Oncogene:*** A gene that under certain circumstances has the potential to cause cancer.
Dominant negative mutation: Mutations resulting in an altered gene product that acts antagonistically to the wild-type protein. These mutations usually result in an altered molecular function (usually inactivation) and are characterized by a dominant or semi-dominant phenotype.	***Predictive biomarker:*** A biomarker which can be used to identify subpopulations of patients who are most likely to respond to a given therapy.
Driver mutations: Mutations that are causally implicated in oncogenesis.	***Prognostic***: A biomarker that provides information on the likely course of disease.
Early termination mutation: A mutation that results in a premature stop codon, or a nonsense codon in the transcribed messenger RNA, and a truncated, often nonfunctional protein product.	***Proteomics:*** Systematic and large-scale study of proteins and their structures and functions.
Epigenomics: The study of epigenetic modifications (such as DNA methylation).	***Silent mutation:*** Mutations in DNA that do not change the amino acid sequence of the protein product of the gene.
Exome: The part of the genome formed by exons, the sequences which when transcribed remain within the mature RNA after introns are removed by RNA splicing.	***Somatic mutation:*** Alterations in DNA that occur after conception. These mutations are not passed on to the offspring. These alterations may result in cancer and other diseases.
Exosomes: Small membrane vesicles of endocytic origin, thought to play important roles in intercellular communications.	***Targeted sequencing:*** Sequencing focused on a limited number of genes.
Germline mutation: A heritable variation in the genetic material of germ cells that is transmittable to the offspring.	***Tumor suppressor gene:*** A gene that protects the cell from a step down the path toward cancer (such as *TP53* protecting genomic integrity).
Hot-spot mutations: Mutations in regions of DNA that occur with an unusually high frequency. Hot-spot mutations in cancer usually provide a selective growth advantage to neoplastic cells.	***Whole-exome sequencing:*** A sequencing procedure by which the sequence of all protein coding regions of the DNA (exons) from a single individual are interrogated.
Metabolomics: The systematic study of the metabolites present within an organism, cell, or tissue.	***Whole-genome sequencing:*** A sequencing procedure by which the entire genome is interrogated thereby determining the complete DNA sequence of the genome of a single individual.