

# Cancer Genetics Laboratory

## **Cancer Exome Sequencing**

**The Cancer Exome Sequencing (CES)** test is a complex test developed to identify changes in a patient's tumor DNA that can be used to predict tumor behavior or determine the likelihood of response/resistance to targeted agents or other forms of cancer therapy. This test applies the power of next-generation sequencing technology to cancer genetics in a CAP/CLIA -approved setting with clinical interpretation of the sequence information.

**The Exome:** The term exome refers to the portion of the human genome that contains the DNA sequence that directs protein synthesis. These functionally important regions of DNA are referred to as exons. The 22,000 known genes are comprised of approximately 180,000 exons and represent about 3% of the genome. Most errors in a DNA sequence that lead to altered protein function in tumors are located in the exons, therefore, exome sequencing is an efficient method for tumor DNA sequence analysis to uncover genetic causes for tumor behavior.

**Reporting of the Test:** The Cancer Exome Sequencing test reports all somatic mutations identified in the tumor exome and classifies them according to clinical utility based on careful evaluation of functional and clinical evidence in the medical/ scientific literature and the availability of agents targeted to a specific gene or pathway. This test also reports the presence of germline (inherited) genetic variations in selected genes known to increase the risk for cancer. The mutations will be categorized into the following groups based on these criteria:

- **Category IA.** Somatic (acquired) sequence variants that have been established as diagnostic, prognostic and/or predictive of treatment response in the tumor type being tested, following clinical practice guidelines (ASCO, NCCN, etc.) or recommendation of the BCM Genomics tumor board. *Examples: BRAF, FLT3, KRAS*
- **Category IB.** Germline (inherited) sequence variants in cancer susceptibility genes that have been reported as pathogenic or likely pathogenic in HGMD, locus specific databases or peer-reviewed literature. *Examples: APC, TP53, VHL*
- **Category II.** Somatic (acquired) sequence variants in genes that are members of cancer pathways, gene families, or functional groups/pathways that are targets of approved or investigational therapeutic agents. *Examples: AKT, FGFR1, PIK3CA*
- **Category III.** Somatic (acquired) sequence variants in consensus cancer genes as defined by the Wellcome Trust Sanger Institute Cancer Gene Census or the BCM Genomics Tumor Board. These are genes in pathways that are not currently considered druggable.
- Category IV. Somatic sequence variants not included in Categories I-III.





### **TECHNICAL INFORMATION**

**Principle of the Test:** The principle of the test is to sequence nucleotide by nucleotide, the human exome of normal tissue (generally blood) and a sample of tumor tissue to a depth of coverage necessary to determine sequence variations that are unique to the tumor (somatic mutations) with high sensitivity. Point mutations, insertions and deletions of the exome are potentially discoverable and could be considered important for cancer management depending on the defect and available evidence. These sequence variations are then categorized based on their role in defining a specific tumor property or tumor sensitivity to established and novel therapeutic approaches. Somatic mutations with established and potential clinical utility, as well as cancer susceptibility germline variants, are confirmed by a second sequencing method.

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#### **Test Details:**

200X Average Coverage ~98% Coverage of Categories I and II Genes 3058 of Most Commonly Mutated COSMIC Genes are Fully Covered 81 Hereditary Cancer Predisposition Genes Evaluated

#### **ORDERING THE CANCER EXOME SEQUENCING TEST**

**Indications for Testing:** The Cancer Exome Sequencing test is ordered by a physician. In general, the test is used when a patient's oncology management would benefit from identifying genetic changes in the tumor that predict sensitivity or resistance to a variety of therapeutic regimens. In some cases, the test could be ordered to understand the genetic complexity of a tumor in order to better predict a patient's possible clinical course.

Specimens: Two specimen types required for this test.

Specimen Type of Normal Tissue:	Blood, Cultured Skin Fibroblast, Purified DNA (6 μg)
Specimen Type of Tumor Tissue:	Fresh Frozen Tissue (200 mg), Purified DNA (6 µg)

**Forms:** Requisition, patient intake and signed consent form must accompany specimen. Prior to any genetic testing, we recommend discussion of the risks and benefits of testing with a physician and/or genetic counselor. To receive our forms, additional information, or kits, please contact our laboratory: 1-877-798-1063 and www.cancergeneticslab.org.

**Shipping Address:** Baylor College of Medicine, Cancer Genetics Laboratory, 2450 Holcombe, Grand Blvd. - Receiving Dock, Houston, Texas 77021-2024.

