CARIS MI®
MOLECULAR INTELLIGENCE

Now Reporting – Genomic Loss of Heterozygosity

Caris Life Sciences® utilizes MI Exome™ (whole exome sequencing) to analyze 250,000 evenly-spaced single nucleotide polymorphisms (SNP) to measure genomic instability in the tumor. Genomic Loss of Heterozygosity (LOH) or genomic instability is often related to defective homologous recombination repair mechanisms. High levels of genomic instability may be indicative of PARP-inhibitor and platinum therapy response.

Genomic LOH testing is provided at no additional cost and no increase in specimen requirements or turnaround time when MI Profile™ or MI Tumor Seek™ are ordered. The results can be found in the Genomic Signatures section of the Caris Molecular Intelligence® report, alongside Microsatellite Instability (MSI) and Tumor Mutational Burden (TMB) results.

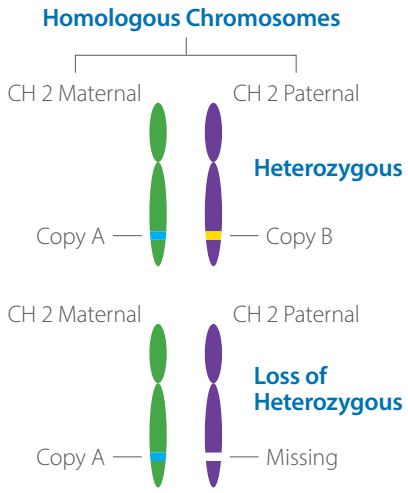
Genomic Signatures

Biomarker	Method	Analyte	Result
Genomic Loss of Heterozygosity (LOH)	Seq	DNA-Tumor	High - 38% of tested genomic segments exhibited LOH (assay threshold is ≥ 16%)

With the addition of genome-wide LOH reporting to the company's existing whole exome, whole transcriptome sequencing and proteomic testing services, as well as advanced AI and machine learning capabilities, Caris Molecular Intelligence remains the most comprehensive and clinically relevant molecular profile for cancer patients in the industry.

What is Loss of Heterozygosity (LOH)?

- **Normally, there are 2 copies of every gene in a person's DNA (excluding sex chromosomes in males)**
- **When the copies are not identical, the person is considered heterozygous at that gene location**
- **In cancer, DNA damage events can occur in the cell that causes the loss of one copy**
  - In the second example shown here, the cell has lost copy A and, therefore, is no longer heterozygous at this location.
- **LOH can occur at the single-gene level or genome wide - which is called Genomic LOH**
  - Single-gene level: In a person heterozygous for a tumor suppressor gene (one functional copy and one disabled copy), the loss of the functional copy can lead to cancer, as the person no longer has a working version of the tumor suppressor.
  - Genome-wide: When a person has lost a critical gene involved in DNA repair, chromosome deletions can appear throughout the genome, resulting in LOH at thousands of locations. Even if the DNA repair gene alteration is missed in testing, the detection of genomic LOH can identify a tumor that may be susceptible to drugs that impact the DNA-damage/repair pathway (PARP inhibitors or platinum agents).
  - The Caris assay measures genomic LOH in order to identify cases of potential homologous-recombination deficiency that are not identified with standard NGS.



The cell has lost copy B and, therefore, is no longer heterozygous at this location.

Genomic LOH reporting is not available in New York State.

To order or learn more, visit **www.CarisMolecularIntelligence.com.**
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