Belay Ascent™

Proprietary Sequencing for Aneuploidy in CSF

BELAY DIAGNOSTICS

Ascent assesses chromosome arm-level and focal losses and gains via low-pass whole genome sequencing (LP-WGS) of tumor-derived nucleic acid in CSF to help inform the diagnosis and management of confirmed or suspected primary and secondary CNS malignancies.

A highly sensitive approach to evaluating chromosome arm-level and focal losses and gains in CSF-derived nucleic acid

WHY CHOOSE BELAY ASCENT?

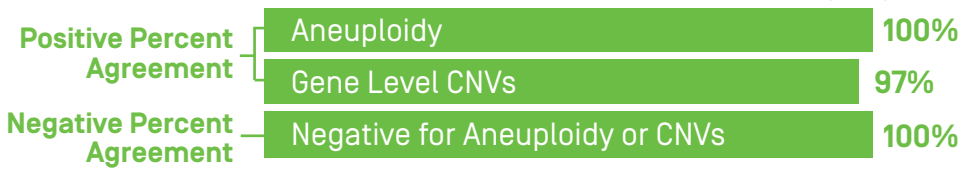
1. Ascent is highly sensitive, using low amounts of input nucleic acid.
2. Ascent employs proprietary technology exclusively licensed for use in CSF by Belay Diagnostics to detect chromosome arm-level and focal losses and gains in confirmed or suspected CNS cancers.
3. Pairing Ascent with Summit™ 2.0 can provide critical information for informing the diagnosis and management of CNS cancers using a single CSF specimen.*

Biologic and Technical Basis: Arm-Level Alterations in CNS Malignancies

- Primary and metastatic CNS cancers can be detected by interrogating CSF for chromosome arm-level and focal losses and gains, which occur in most CNS cancers.[1,2]
- CSF-based methods for detection of these alterations use low input nucleic acid and have shown superior sensitivity to the gold-standard of CSF cytology.[2]

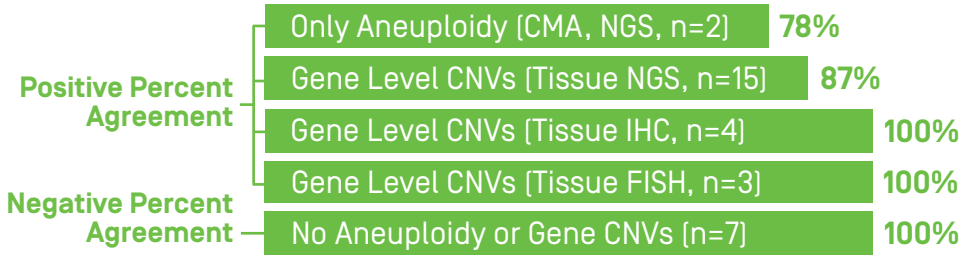
ASCENT™ DEMONSTRATES EXCEPTIONAL EQUIVALENCE TO STANDARD METHODS

% Concordance of events: Ascent™ to CMA/NGS, Tissue (n=48)



ASCENT™ IN CSF IS HIGHLY CONCORDANT TO TISSUE

% Concordance of events: Ascent™ in CSF to Tissue Profiling (n=32)



*See Sample Requirements on page 2 for more details

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Tumor-Specific Chromosomal Signatures and Clinical Differentiation

- Some primary CNS cancers can be identified by characteristic conserved patterns of arm-level losses or gains:
  - Glioblastomas are characterized by Chr. 7p,q gains and Chr. 10 p,q losses[1,2]
  - IDH-mutant oligodendrogliomas canonically exhibit co-deletion of Chr. 1p and Chr. 19q[2]
  - Meningiomas are risk-stratified by arm losses[3]
  - Medulloblastomas are characterized by chromosome arm loss and gain rather than mutations in specific genes[4]
- GBM and CNS lymphoma can appear similar in imaging but have drastically different patterns of chromosomal loss and gain. Accurate characterization is critical; these cancers have significantly different treatment[2]
- Cancer of the breast, lung, and melanoma are most likely to metastasize to the CNS; each has shown chromosome arm-level loss and gain detectable in CSF-tDNA[1,2]
- Identifying chromosomal alterations can aid in distinguishing neoplasia versus non-neoplastic disease when other tools yield non-diagnostic or negative results[2]

Assay Specifications

Clinical Performance	Whole arm-level and focal losses and gains on all chromosomes (only q arms for acrocentric chromosomes 13, 14, 15, 21, and 22)
Sample Requirements	≥ 6 mL of CSF*. A sample of < 6ml of CSF will be processed and results reported provided the sample meets established reporting thresholds
Shipping and Transport Temperature	Standard CSF collection tube. Must be shipped in Belay Diagnostics specimen shipping kit within 24 hours of CSF collection and received at Belay Diagnostics within 48 hours. Maintain specimen at room temperature. Do not freeze or refrigerate **unless instructed to do so.**
Methodology	Low-pass whole genome sequencing
Orders and Results	Include test requisition in shipping kit or fax form to 800-501-9246. Test results available via fax, encrypted email, or Belay portal.
Turnaround Time	Average 7-10 days from receipt of specimen

References: 1. Douville C, Curtis S, Summers M, Azad TD, et al. Seq-ing the SINEs of central nervous system tumors in cerebrospinal fluid. Cell Rep Med. 2023 Aug 15;4(8):101148. doi: 10.1016/j.xcrm.2023.101148. Epub 2023 Aug 7. PMID:37552989; PMCID: PMC10439243. **2.** Zheng Y, Ahmad K, Henikoff S. Total whole-arm chromosome losses predict malignancy in human cancer. Proc Natl Acad Sci U S A. 2025 May 6;122(18):e2505385122. doi: 10.1073/pnas.2505385122. Epub 2025 May 2. **3.** Liu APY, Smith KS, Kumar R, Paul L, et al. Serial assessment of measurable residual disease in medulloblastoma liquid biopsies. Cancer Cell. 2021 Nov 8;39(11):1519-1530.e4. doi: 10.1016/j.ccell.2021.09.012. Epub 2021 Oct 21. **4.** Sahm F, Aldape KD, Brastianos PK, Brat DJ, et al. cIMPACT-NOW update 8: Clarifications on molecular risk parameters and recommendations for WHO grading of meningiomas. Neuro Oncol. 2025 Feb 10;27(2):319-330. doi: 10.1093/neuonc/noae170. **5.** Nie Q, Schilter KF, Hernandez KM, Adams JN, et al. Analytical Validation and Clinical Sensitivity of the Belay Summit Assay for the Detection of DNA Variants in Cerebrospinal Fluid of Primary and Metastatic Central Nervous System Cancer. J Mol Diagn. 2025 Jul;27(7):615-629. doi: 10.1016/j.jmoldx.2025.03.010. Epub 2025 Apr 23.

This test was developed, and its performance characteristics determined by Belay Diagnostics, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes.

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