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 tumor-derived nucleic acid

WHY CHOOSE BELAY ASCENT?

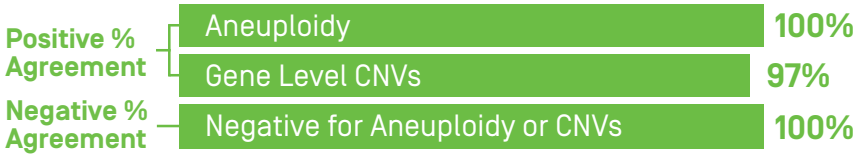
1. Ascent is highly sensitive, using low amounts of input nucleic acid.
2. Ascent employs proprietary technology exclusively licensed for use in CSF by Belay Diagnostics to detect chromosome arm-level and focal losses and gains in confirmed or suspected CNS cancers.
3. Pairing Ascent with Summit™ 2.0 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]

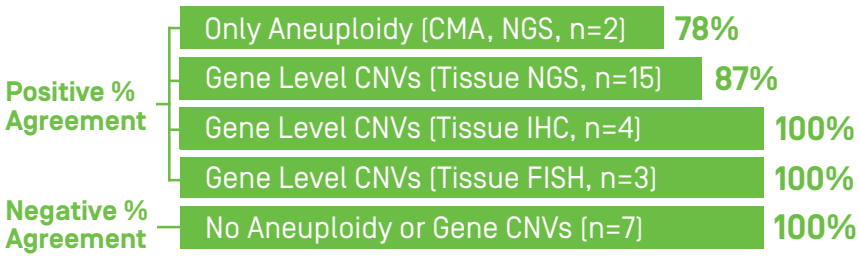
ASCENT™ DEMONSTRATES EXCEPTIONAL EQUIVALENCE TO STANDARD METHODS

% 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, 22)
Collection and Sample Requirements	Collect ≥ 6 mL of CSF in your institution's standard CSF tubes. Samples < 6 mL will be processed and results reported if established reporting thresholds are met. Wrap tubes in Parafilm, if available, to prevent leakage. Label each tube with the collection date and two unique patient identifiers matching those on Test Requisition Form (TRF).
Temperature Control	**Shipping within 24 hours of collection**: Maintain specimens at room temperature. Specimens must be received at Belay within 4 calendar days of collection. **Shipping 1-3 days after collection**: Refrigerate within 4-6 hours of collection. Ship at ambient temperature. Specimens must be received at Belay within 2 calendar days of shipment. **Shipping after more than 3 days**: Freeze at -80°C within 4-6 hours of collection. Ship on dry ice. Note, frozen samples cannot be shipped in Belay shipping kits and require alternate shipping containers provided by the client.
Packing and Shipping	Open Belay shipping kit and remove contents. Activate temperature tracker and attach to biohazard bag. Insert labeled tubes into absorbent sleeve, place in biohazard bag, and seal. Wrap the gel blanket around the biohazard bag, place inside Styrofoam container, and close lid. Place the TRF, signed informed consent, and any clinical reports on top of Styrofoam container and close outer lid. Place kit inside provided FedEx bag, seal, add FedEx label, and schedule pickup or include in your standard pickup procedures.
Methodology	Low-pass whole genome sequencing
Orders and Results	Include TRF in shipping kit or fax form to 800-501-9246. Test results available via fax, encrypted email, or Belay portal.
Turnaround Time	Average 10-14 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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