

HistioTrak Qualitative Droplet Digital PCR



Langerhans cell histiocytosis (LCH), disseminated juvenile xanthogranuloma (JXG) family neoplasms, and pediatric Erdheim-Chester disease (ECD) are myeloid-derived clonal inflammatory disorders driven by recurrent kinase-activating mutations, most frequently in the MAPK signaling pathway. BRAF p.V600E is a hotspot mutation that strongly activates the MAPK pathway and is commonly harbored by multiple tumors, including histiocytic, hematopoietic, brain, papillary thyroid, and melanocytic neoplasms. It is the most prevalent mutation in LCH and ECD, carries prognostic significance, especially in multisystem LCH, and is a stable marker of histiocytoses that can be leveraged as an indicator of minimal residual disease (MRD). Targeted therapy with MAPK pathway inhibitors has been highly effective in the treatment of histiocytosis with mutations in pathway genes, including the BRAF p.V600E mutation¹⁻⁵. The HistioTrak test is a highly sensitive droplet digital PCR (ddPCR)-based molecular assay designed to measure MRD in patients with BRAF V600E-driven histiocytic and other neoplasms. It is used for monitoring the disease burden of patients with histiocytosis that harbor a BRAF V600E mutation, during or after therapy. In this setting, it is NOT a diagnostic test. Prior BRAF V600E mutation status should be known before performing the test for whole blood and bone marrow specimens. In select instances, HistioTrak test can be used to determine BRAF V600E mutation status on formalin-fixed, paraffin-embedded (FFPE) tissue specimens, where the BRAF V600E immunohistochemical finding is equivocal or not available. For more information, call the lab at 513-636-9820.

Mutation Target:

BRAF c.1799T>A p.V600E

Reporting Units:

Qualitative: Positive / Suspicious / Negative

Acceptable Specimens:

- 5 mL whole blood or bone marrow in Streck NA BCT tube (preferred; EDTA acceptable only if sample arrives within 24 hours of collection)
- FFPE tissue: 1 H&E slide and 6 unstained slides at 5 microns each
- Paraffin block (block will be returned upon completion of test)

Unacceptable Specimens:

- Decalcified tissue
- Frozen whole blood or bone marrow
- Sample collected in heparin
- Blood or bone marrow specimens collected in EDTA tubes >24 hours old upon receipt

Shipping Conditions:

- Blood and bone marrow samples in EDTA at 4°C in insulated container by **overnight** courier. Do NOT freeze.
- Slides, blocks, or blood and bone marrow in Streck tubes at ambient temperature.
- **For all samples, ship for delivery on Monday through Friday. Receiving docks are CLOSED on weekends and holidays; do NOT ship if delivery will occur on those days.**

Testing Schedule:

HistioTrak testing is performed Mon-Fri. For testing outside of this schedule, call the lab at 513-636-9820.

TAT: 3-4 business days.

EPIC Test Code:

LAB00421

CPT Codes:

81210 – Testing

G0452 – Physician interpretation

Clinical Lab Index:

HistioTrak:

<https://www.testmenu.com/cincinnatichildrens/Tests/1130008>

Contact Information:

Cincinnati Children's Division of Pathology
Molecular and Genomic Pathology Services (MGPS)

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Email: pathology@cchmc.org

Website: cincinnatichildrens.org/pathology

For pricing or billing questions, call 513-636-4261.

Shipping Address:

Cincinnati Children's Hospital Medical Center
Attn: Molecular and Genomic Pathology Services (MGPS)
3333 Burnet Ave, R2.001
Cincinnati, OH 45229

References:

1. Allen C, et al. *N Engl J Med*. 2018; 379: 856-868.
2. Heritier S, et al. *J Clin Oncol*. 2016; 34: 3023-3030.
3. Picarsic J, et al. *Acta Neuropathol Commun*. 2019; 7:168.
4. Goyal G, et al. *Blood*. 2020; 135: 1929-1945.
5. Lee L, et al. *Blood Adv* 2020; 4: 717-727.