BILLING CODE 4167-05-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government Owned Invention Available for License: Matched Patient-Derived 3D Isocitrate Dehydrogenase (IDH)-Mutant Glioma Cell Lines for Modeling Malignant Transformation

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Cancer Institute (NCI) seeks licensees for matched patient-derived 3D Isocitrate Dehydrogenase (IDH)-mutant glioma cell lines, 403L and 403H, generated from the same patient before and after malignant transformation from WHO grade 2 to WHO grade 4 disease. This research material provides an opportunity to study IDH-mutant glioma progression, temozolomide-associated hypermutation, invasion, metabolism, and treatment resistance.

FOR FURTHER INFORMATION CONTACT: Inquiries related to this license opportunity should be directed to: Michael Pollack, Unit Supervisor, NCI, Technology Transfer Center, Email: *michael.pollack@nih.gov* or Phone: 240-276-5519.

SUPPLEMENTARY INFORMATION: IDH-mutant gliomas often begin as lower-grade tumors but remain incurable and frequently progress to higher-grade disease through malignant transformation. This is clinically important but difficult to study because matched low-grade and high-grade tumor materials from the same patient are rare. Further, fixed tumor specimens are limited for repeated mechanistic or drug-response experiments.

Researchers at the NCI developed a matched pair of patient-derived cell models, 403L and 403H, from the same patient before and after malignant transformation. 403L was established from a WHO grade 2 IDH-mutant astrocytoma. 403H was derived from the recurrent WHO grade 4 tumor following radiation and temozolomide treatment. Both cell lines: (1) grow as 3D spheroids, (2) retain endogenous IDH1 R132H expression, and

(3) were authenticated to the patient's germline by short tandem repeat (STR) profiling (100% match for 403L; 93.33% match for 403H).

The high-grade 403H line shows increased invasive behavior, temozolomide-associated hypermutation (tumor mutational burden of 70.07/Mb vs. 3.96/Mb in 403L), upregulated epithelial-mesenchymal transition (EMT) signaling (whereas Notch signaling is enriched in 403L), and changes in glioma-associated metabolism, including 2-hydroxyglutarate (2-HG), glutamine, fatty acid metabolism, and lactate/pyruvate flux. Furthermore, 403H showed significantly greater 3D invasion than 403L ($p<0.0001$). 403H formed infiltrative high-grade glioma in 4 of 5 orthotopically xenografted NSG mice. In contrast, 403L did not form tumors within 18 months.

"This Notice is in accordance with 37 C.F.R. § 404.4 Authority to grant licenses."

NIH Reference Number: E-145-2026-0.

Related Technologies: N/A.

Product Type: Research Material/Tool.

Therapeutic Area(s): Oncology | Neurology.

Development Stage: Developed

Publications:

- Kim O, et al. A patient-derived cell model for malignant transformation in IDH-mutant glioma. (https://pubmed.ncbi.nlm.nih.gov/39256867/)

Patents: PCT/US2024/054179, filed November 1,2024.

Potential Commercial Applications:

- Molecular classification and diagnosis of CNS and kidney tumors, including difficult-to-classify and low-confidence cases.
- Diagnostic subtyping aligned to WHO-guided entities.
- Reference-lab and hospital-lab deployment.
- Clinical trial stratification and translational research cohort harmonization.
- Multi-classifier diagnostic decision support.
- Cancer treatment development.

Competitive Advantages:

- Developed from a rigorously curated, large reference set of methylation profiles.
- Clinically relevant CNS diagnostic.
- CNS tumor methylation classes not represented in existing tools, expanding diagnostic coverage.
- Clinical-impact analysis creating superior diagnostic precision.
- Superior classifier for kidney cancer.
- Superior classifiers for multiple solid, difficult-to-diagnose tumors.
- Integrative into clinical workflows, improving diagnostic practices and enhancing patient care.

Dated: August 19, 2026.

Richard U. Rodriguez,

Associate Director,

Technology Transfer Center,

National Cancer Institute.

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