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# Systematic Review of Cerebrospinal Fluid Biomarker Discovery in Neuro-Oncology: A Roadmap to Standardization and Clinical Application

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## Abstract

Effective diagnosis, prognostication, and management of CNS malignancies traditionally involves invasive brain biopsies that pose significant risk to the patient. Sampling and molecular profiling of cerebrospinal fluid (CSF) is a safer, rapid, and noninvasive alternative that offers a snapshot of the intracranial milieu while overcoming the challenge of sampling error that plagues conventional brain biopsy. Although numerous biomarkers have been identified, translational challenges remain, and standardization of protocols is necessary. Here, we systematically reviewed 141 studies (Medline, SCOPUS, and Biosis databases; between January 2000 and September 29, 2022) that molecularly profiled CSF from adults with brain malignancies including glioma, brain metastasis, and primary and secondary CNS lymphomas. We provide an overview of promising CSF biomarkers, propose CSF reporting guidelines, and discuss the various considerations that go into biomarker discovery, including the influence of blood-brain barrier disruption, cell of origin, and site of CSF acquisition (eg, lumbar and ventricular). We also performed a meta-analysis of proteomic data sets, identifying biomarkers in CNS malignancies and establishing a resource for the research community.

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