TERT Promoter Mutation for Glioma Prognosis

TERT promoter mutation, in concert with *IDH1/2* mutation status and chromosome 1p/19q FISH results, impact prognosis in patients with diffuse glioma**.**

Pathobiology:

The enzyme telomerase is required for maintenance of telomere length in dividing cells. Normal cells typically lack telomerase, but in some cancers, telomerase is activated by point mutation within the *TERT* gene promoter. The mutation is typically located 124 or 146 base pairs upstream of the transcriptional start site (known as -124C>T and -146C>T, or colloquially called C228T and C250T).

In glioma, the combination of *TERT* promoter, *IDH1/2*, and chromosome 1p/19q mutation status can identify prognostically-distinct molecular subgroups. In particular, grade 2 or 3 glioma harboring *TERT* promoter mutation, wild-type *IDH1/2,* and lacking 1p/19q deletion has a very poor prognosis comparable to that of glioblastoma (grade 4).

TERT promoter mutation is seen in many other cancer types, and studies are underway to assess impact on patient management.

Test Indication: Prognosis of grade II or III glioma.

Specimen Requirements:

This assay uses genomic DNA extracted from paraffin-embedded tumor tissue. Ten unstained slides from a diagnostic block should be submitted, along with an H&E stained slide marked by the pathologist to indicate the most tumor-rich region (at least 50% tumor nuclei required). After macrodissection and DNA extraction, the *TERT* promoter region is analyzed by Sanger sequencing. Results at positions -124C>T and -146C>T are interpreted by a pathologist.

References:

Eckel-Passow JE, *et al. "*Glioma groups based on 1p/19q, *IDH*, and *TERT* promoter mutations in tumors." *New Engl J Med.* 2015; 372(26): 2499-2508. PMID: 26061753.

Griewank KG, *et al. "TERT* promoter mutation status as an independent prognostic factor in cutaneous melanoma." *J Natl Cancer Inst.* 2014. 106(9). PMID: 25217772.

Vinagre J, *et al.* "Telomerase promoter mutations in cancer: an emerging molecular biomarker?" *Virchows Arch.* 2014; 465(2): 119-133. PMID: 25048572.

To consult a pathologist about indications for testing or the significance of a result, call the Molecular Genetics Lab at (984) 974-1825 or Dr. Gulley at (919) 843-4595. E-mail: margaret_gulley@med.unc.edu

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