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Publication(s)

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External Link(s)

• From the lab of Dr. Hai Yan
• u201cPromoting a new brain tumor mutation: TERT promoter mutations in CNS tumors.u201d (Acta Neuropathologica, 2013).
• u201cThe implications of IDH mutations for cancer development and therapy.u201d (Nature Reviews Clinical Oncology, 2021).
• u201cThe genomic landscape of TERT promoter wildtype-IDH-wildtype glioblastoma.u201d (Nature Communications, 2018).
• u201cRecurrent TERT promoter mutations identified in a large-scale study if multiple tumour types are associated with increased TERT expression and telomerase activation.u201d (European Journal of Cancer, 2015).
• u201cMutations in IDH1, IDH2, and in the TERT promoter define clinically distinct subgroups of adult malignant gliomas.u201d (Oncotarget, 2014).

Rapid detection of diagnostic TERT promoter mutations in glioblastoma and other cancers

Unmet Need

Malignant gliomas are the most common primary central nervous system (CNS) malignancy in adults and are graded I to IV indicating their degree of malignancy. Diffuse gliomas (grade II-IV) account for 80% of primary brain tumors and cannot be cured with surgical resection. Patient outcome can vary significantly between glioma subsets. However, accurate diagnosis of diffuse glioma is challenging due to heterogeneity, invasiveness, and ambiguity among morphological features. Accurate diagnosis is important for treatment decision making, and objective, tumor-specific markers are needed for design of personalized care for patients. Sequencing studies have identified common genetic mutations that can be used to classify gliomas including mutations in *IDH1/2* and the *TERT* promoter. Current sequencing methods are limited by poor sensitivity which affects diagnosis. There is a need for rapid and highly specific detection of *TERT* promoter and *IDH1/2* mutations in glioblastoma and other TERT-high tumor types.

Technology

Duke inventors have developed a highly sensitive quantitative PCR (qPCR)-based assay to detect specific genetic mutations in cancer. This is intended to be used in the diagnosis and classification of diffuse malignant gliomas to help guide treatment decisions for patients. These alterations are also present in a number of other cancers, in particular the *TERT* promoter mutation. Specifically, this assay is used to detect C228T and C250T mutations in the *TERT* promoter, R132 mutations in *IDH1*, and R172 mutations in *IDH2*. Due to this assay's sensitivity, mutations can be detected in circulating tumor DNA (ctDNA) isolated from liquid biopsy samples as well as tumor tissue, margin tissue, and metastatic samples. The assay uses heterozygous calibrator plasmids to specifically amplify the target genetic regions and locked nucleic acid (LNA) primers to enhance specificity. This has been demonstrated in diverse diffuse-type glioma tumor samples and other TERT-high cancers.

Other Applications

This technology could also be used in the diagnosis of other TERT-high tumor types including melanoma, urinary tract carcinoma, other CNS tumors, hepatocellular carcinoma, myxoid liposarcoma and oral cavity carcinoma.

Advantages

- Highly sensitive and specific for selective genomic regions compared to standard Sanger sequencing methods
- Faster and simpler than assays with comparable sensitivity; can be done in a few hours with a single PCR step

Amenable to diverse sample types including tumor tissue and liquid biopsies