Unmet Need
Glioblastoma is the most common type of malignant brain tumor, and accounts for 47.7% of all brain cancer cases. Despite aggressive treatment, the median overall survival for glioblastoma is 15 to 18 months. Currently, prognosis and treatment approaches are based on sets of robust biomarkers that define the type of glioblastoma. Two major biomarkers are the presence of mutations in the genes IDH, leading to widespread tumorigenic changes in the epigenome, and the promoter of TERT, which lead to increased TERT expression and telomerase activation to maintain telomeres. However, this set of biomarkers is unable to identify glioblastomas that do not have these mutations, which accounts for approximately 20% of all glioblastomas. These patients may therefore not receive optimal treatment given their disease biology may be different. There is a need for more comprehensive molecular markers for glioblastoma to improve personalized diagnosis and treatment, as well as aid research and development of novel therapeutics.

Technology
Duke inventors have developed a set of biomarkers that identify subtypes of glioblastoma. This is intended to be used to identify the subtype of glioblastoma that is currently not captured by existing biomarkers and to aid in diagnosis and treatment. Specifically, Duke inventors have discovered that this previously undefined subset of glioblastoma had mutations outside of the classic glioblastoma biomarkers, the TERT promoter mutations and IDH mutations. These newly discovered mutations in this subgroup of glioblastoma have mutations which either moved TERT to another
chromosomal position, altering the expression of TERT, or caused changes in other genes (ATRX or SMARCAL1) which activated a telomerase-independent mechanism of telomere maintenance known as alternative lengthening of telomeres (ALT). This has been demonstrated in whole genome and exome sequencing of tumor samples from glioblastoma patients and validated in vitro using cell lines.

**Other Applications**

This technology could also be used to develop novel therapeutics for the treatment of glioblastoma.

**Advantages**

- Identifies new drug targets for glioblastoma.
- Classifies a previously unclassifiable subset of glioblastoma.
- Adds another modality to the treatment of glioblastoma.