**Methods**

Glioblastoma Multiforme (GBM) is a highly aggressive brain tumor and comprised of heterogeneous genetic profiles making it difficult to target treatment to non-uniform responses and the recurrence of the tumor after treatment. A current obstacle with using conventional MRI to guide a surgical biopsy during tumor resection is that an enhanced tumor area is not always representative of the entire tumor. Consequently, leaving behind brain around the tumor (BAT). BAT is rarely biopsied, but is known to contribute to a recurrence of this tumor (GBM). BAT analysis reveals that 50-60% of patients have GBM heterogeneity resulting from tumor recurrence. This study was designed to characterize the BAT samples from three GBM patients.

**Study Design:** Twelve GBM patients were enrolled by St. Joseph’s IRB-approved protocol prior to their surgical resection for pre-operative multiparameter-NIR and for fluorescent-adapted MR-guided biopsies of the enhancing core and BAT regions, with the final number of biopsies determined during the time of surgery by the neurosurgeon. Due to time and specimen constraints of this subproject, I was only able to complete the analyses of the GBM tumors from three patients. A neuropathologist checked for tissue quality and tumor cellularity of each specimen.

**TGEN acquired the biopsy BAT areas of GBM tissue samples, isolated the DNA, performed the array-based Comparative Genomic Hybridization (aCGH), and analyzed the data received from the aCGH. The primary goal is to assess the differences in the genotypes of tumor cells (Glioblastoma multiforme (GBM) and the cells existing in the core of the tumor. We hypothesized: (1) The BAT genotype will be different from the core of the tumor and we will be able to identify what genomic alterations may explain for the varying recurrence rates.**

**Results**

**Table.** The **Result** sections are divided into two parts: Patient 2 has 3 samples (2 Enh, 1 BAT), Patient 4 has 5 samples (3 Enh, 2 BAT), and Patient 8 has 14 samples (7 Enh, 7 BAT).

**Data Analysis:** TGEN analyzed the data of the aCGH and assessed the GBM that appeared to be aberrant. Hierarchical clustering was used to show relations between samples based on similarity. We used a combination of gene-specific and whole-genome analysis, focusing on a driver of GBM (aCGH). ACGH is a commercialized whole-genome test for Genomic DNA from tumor tissues. This array analysis was used for a drug target of GBM (aCGH). Agilent® Oligonucleotide Array-Based CGH for Genomic DNA analysis from DNA isolation to feature extraction of the array data onto our genomic workbench version 7.0 for use.

**Identified in BAT samples:**

- **Genomic heterogeneity**
- **Heterogeneity for the variants/recurrent tumor.
- **Identified an amplification of chromosome 7 and a deletion of chromosome 10, leading to EGFR gene amplification and PTEN loss, respectively.**

**Conclusions**

GBM is the most common primary central nervous system tumor carrying a poor prognosis. As mentioned above, invasive GBM is currently resistant to therapy, and is the cause of recurrences. GBM heterogeneity and importance of the biopsy among the spatial location of the tumors, specifically with BAT samples. An increase in amplification of genes involving the VHL-RAS-pathway and BAT and/or BAT samples were observed, which promote invasion and migration, also known as, mesenchymal-endothelial transition. Currently, a biopsy can miss the portion of the tumor that is not susceptible to the specific treatment, especially in GBMs. Recent studies have identified the genetic drivers of regions of BAT, which are regions rather difficult to visualize during surgery. We identified this concept’s resistance to conventional therapies. As such, the future direction of this study is aimed to non-invasively identify the genomic profile of patients phenotypically via MRI. This study is a valuable approach in patient specific care, treatment, and outcome.

**Dedication & Acknowledgements**

**Dedication:** Dedicated to the memory of my loving grandmother, Wanda Ford. She is one of many who lost their life too young due to GBM. I would like to thank Dr. Tran and his colleagues for the opportunity to work with them on this project that will greatly benefit the GBM community.

**Acknowledgments:** I would like to thank my mentor, Dr. Nhan Tran, and his colleagues at TGEN’s Brain Tumor Labs. I wish to thank Dr. Tran and his colleagues the best of luck with the continued R21 project.

**References:**

1. Barbee, N., Tran, N., and TGEN. The cadherins to bind together at the cytoskeleton junction.

2. Glioblastoma Multiforme (GBM) is a highly aggressive brain tumor and comprises of heterogeneous genetic profiles making it difficult to target treatment to non-uniform responses and the recurrence of the tumor after treatment.

3. A current obstacle with using conventional MRI to guide a surgical biopsy during tumor resection is that an enhanced tumor area is not always representative of the entire tumor. Consequently, leaving behind brain around the tumor (BAT). BAT is rarely biopsied, but is known to contribute to a recurrence of this tumor (GBM).

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9. **Results**

- **Data Analysis:** TGEN analyzed the data of the aCGH and assessed the GBM that appeared to be aberrant. Hierarchical clustering was used to show relations between samples based on similarity.

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- **Agilent® Oligonucleotide Array-Based CGH for Genomic DNA analysis from DNA isolation to feature extraction of the array data onto our genomic workbench version 7.0 for use.**

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