BI-23. LOSS OF NOVEL lncRNA DEFINES THE GLIOBLASTOMA MESENCHYMAL SUBTYPE
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Glioblastoma multiforme (GBM) is one of the most common brain tumors and the first cancer studied by The Cancer Genome Atlas (TCGA). GBM is a very aggressive disease with one of the worst 5-year survival rates among all human cancers. Molecular analysis has revealed several intrinsic subtypes based on gene expression relevant for GBM, including the mesenchymal subtype. Long non-coding RNAs (lncRNAs) have not been well studied in GBM and their function is largely unknown. A custom RNA-seq preprocessing pipeline was used on GBM primary tumor samples to extract lncRNA expression with respect to the mesenchymal subtype. We used the STAR algorithm in combination with the Gencode lncRNA database to derive lncRNA expression calls. Next, we used the FeatureCounts algorithm to quantify the expression calls. The counts were normalized using the DESeq2 rlog transformation algorithm. After alignment using STAR, 101 samples passed the 75% alignment filter, representing all gene expression subtypes. Next, using FeatureCounts, we had expression calls for 6667 lncRNAs. After removing lncRNAs with variance below .01, there were 4433 lncRNAs with expression counts across all samples. Out of the top 10 varying lncRNAs, a lncRNA with unknown function was significantly negatively correlated with the mesenchymal subtype (p-value of 9.4E-05). Next, we used k-means clustering on the top 4000 most varying coding genes to divide them into co-expressed clusters, or metagenes. We correlated the novel lncRNA with these metagenes to identify its function. The top positively correlated metagene was enriched in neurogenesis, neuron differentiation and neuron apoptosis. We identified a potential role for a novel lncRNA strongly related to the mesenchymal subtype and crucial for normal neurogenesis. We hypothesize that this lncRNA is essential for neurogenesis and must be removed for glioblastomas to undergo neural to mesenchymal (NMT) transition.