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Examining Roles of Transposable Elements and DNA Methylation in Glioblastoma

You Rim (Mikayla) Choi
Washington University in St. Louis

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Mentor: Ting Wang

Transposable elements (TEs) have the ability to move from one chromosomal location to another, contributing to genetic variation over evolutionary time. Although TEs make up roughly half of the human genome, TEs were long considered to be junk DNA due to their repetitive nature and their epigenetically silenced state. However, recent discoveries suggest that TEs are still functionally potent because their innate on/off regulatory potential may shape cell development. Specifically, hypomethylated TEs, present due to aberrant methylation machinery or changes that accumulate through natural selection, can regain regulatory function and promote misregulation of nearby genes, which potentiates tumorigenesis. For example, TEs can function as a novel promoter if their endogenous promoters are reactivated. Furthermore, TEs may act as an enhancer, which promotes transcription through transcription factor binding, or as an insulator, by inhibiting transcriptional chromatin domains. Although few examples of TE misregulation-causing cancer have been well documented, TE's role in glioblastoma development is still an uncharted field. Here, we propose to characterize TE's DNA methylation state across three glioblastoma stem cell lines derived from primary tumors. We will compare methylation profile of fetal brain to glioblastoma samples to identify glioblastoma-specific TE misregulation by utilizing bisulfite sequencing technology and various analysis softwares. We hypothesize that changes in DNA methylation of specific transposable elements could be responsible for the oncogenic potential in primary glioblastoma.