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Differential methylation patterns between AML and healthy patients

{Placeholder for hook, maybe mention the percentage of AML patients with significant changes to their methylation profile}. With an estimated 21,380 cases in 2017, Acute Myeloid Leukemia accounted for 1.3% of all new cancer cases and was the cause of 10,590 deaths, accounting for 1.8% of cancer-related deaths. [[1]](#footnote-1) While patients with AML generally have fewer genetic mutations than patients with other cancers, epigenetic modifications, primarily DNA methylation, has been implicated as a major driver in the development of de novo cases[[2]](#footnote-2) and the level of methylation/epigenetic differences is often used in prognosis development.[[3]](#footnote-3) While many differentially methylated regions (DMRs) have been found in patients with AML as opposed to healthy patients, no study has focused on the differences in methylation profiles between known oncogenes in AML and other, unrelated genes. A comprehensive, gene-region focused understanding of the differential methylation in profiles of AML patients may help identify causes and potential treatments for AML that have previously been missed.

Previous studies have focused on the identification of DMRs between patients with AML and health patients; however, these studies have not looked at the methylation profile between these two groups while considering the genes’ role in carcinogenesis. We will study the difference in methylation profiles of oncogenes and non-related genes between these two sets of patients by collecting, normalizing, and annotating methylation bead chip data from TCGA. After assembly of our data, we will focus on identifying difference in methylation profiles between groups of genes in our two patient groups. The feasibility of the project is supported by previous endeavors to analyze the TCGA AML methylation data for various studies. Analyzing the methylation profile of the TCGA data within the aforementioned clustering model is expected to yield differences that are normally masked by typical “bump-hunting” methods. This approach will allow for further exploration of the effect of differential methylation on the development of AML and similar cancers.

Aim 1 will collect the TCGA, perform normalization methods on the data, and annotate the data with genomic region information. Assembling using previously developed pipelines and a myriad of well-documented normalization methods will provide a reliable dataset for analysis that may be repeated with similar sets of data.

Aim 2 will analyze the differential methylation profiles of known AML oncogenes and non-related genes between AML and healthy patients. By looking for a comprehensive profile within these groups, other indicators of change in the normal profile, such as variability, may be found that would otherwise be missed by existing methods.

The proposed study will establish a differential methylation analysis method that takes into account known information about the disease and the clustering of methylation profiles. This method will provide further insight into the effects and patterns of abhorrent methylation in AML. This will prove to not only be useful for the continued study of AML, but may also prove useful when studying other cancers/diseases that have a known or suspected epigenetic relation.

1. https://seer.cancer.gov/statfacts/html/amyl.html [↑](#footnote-ref-1)
2. http://www.nejm.org/doi/full/10.1056/NEJMoa1301689 [↑](#footnote-ref-2)
3. http://www.pnas.org/content/114/28/7414 [↑](#footnote-ref-3)