LARGE SCALE CpG ISLAND METHYLATION PROFILING OF SMALL B CELL LYMPHOMA

Farahnaz B. Rahmatpanah

Dr. Charles W. Caldwell, Dissertation Supervisor

ABSTRACT

DNA methylation plays a significant role in cellular differentiation and biologic activity through silencing of gene expression and also appears to be a factor in the progression of different types of cancer, including Small B cell Lymphomas (SBCL). In this work we utilized three different microarray platforms (9K, 12K and 244K) for the genome wide characterization of DNA methylation in Mantle Cell Lymphoma (MCL), Chronic Lymphocytic Leukemia (CLL), and Follicular lymphoma. The DNA methylation analysis revealed differential methylation patterns in SBCLs. Furthermore, the analysis of DNA methylation profiles suggests that the patterns in CLL may not be homogenous. We demonstrated that the heterogeneity in DNA methylation can be explained, at least in a part, by the CD38 expression levels which is a biomarker to predict the prognosis of the disease in CLL patients. We found alterations in DNA methylation of multiple genes, including *SFRP2, Groucho/TLEs, DKK1, SOX* genes and *APC2* that are members of the WNT signaling pathway in CLL patient samples and CLL cell lines. These genes are viewed as WNT antagonists because of their ability to down regulate WNT signaling. Quantitative real time PCR revealed reactivation of these genes in CLL cell lines after treatment with epigenetic modifying drugs which implies the functional impact of DNA methylation and /or histone deacetylase inhibitors on the mRNA expression of these genes.