Cytosine to Thymine: Unveiling Cancer's Achilles Heel via a Genome-wide Discovery of CpG Methylation Signatures

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Clinical cancer diagnosis faces many challenges, particularly in its low sensitivity and accuracy for early tumor detection. This project aims to develop an early diagnostic platform using leukemia as a model system. Methylation pattern of CpG islands is an epigenetic regulator of gene expression, and extensive alterations of CpG methylation are well documented in cancer. Using genome-wide methylation profiling and machine learning methods, I investigated the ability of CpG methylation status to differentiate acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) from normal blood. Four and seven novel CpG biomarkers were discovered in AML and ALL blood samples, respectively. These methylation panels could distinguish AML or ALL from normal blood with more than 97% accuracy. Importantly, these CpG islands control genes like MNDA, RBP5, TCF25, GDF15, etc. Expression of these genes are down-regulated or up-regulated in leukemia, which is consistent with their CpG methylation profiles. To create a clinically relevant method, a methylation specific PCR prototype was developed and validated targeting these CpG biomarkers. Such a cytosine to thymine nucleotide change at the sequence level enables a rapid and low-cost method for the early screening of leukemia. Moreover, a methylation-based survival classifier was also established that could successfully divide patients into high-risk and low-risk groups, with significant differences of clinical outcome in leukemia subtypes. Together, these findings demonstrate for the first time that CpG panels can be highly sensitive and specific in the accurate diagnosis of AML and ALL with implications for prognosis and treatment selection.

Awards Won:

Intel ISEF Best of Category Award of $5,000

Philip V. Streich Memorial Award to the London International Youth Science Forum

University of the Sciences in Philadelphia: Tuition Scholarship of $15,000 per year for four years.