

Abstract

Development and validation of technologies for large scale epigenetic profiling to study gene-environment interactions

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Introduction: Epigenetic differences in DNA methylation contribute to phenotypic differences between individuals and are an important link between environmental influences and genotypic expression. We planned to compare the effectiveness of profiling genome-wide DNA methylation on a large scale using a chip-based technology (450,000 CpG sites) and a sequencing-based technology (2 million plus CpG sites pulled down and sequenced).

Methods: We have selected 201 subjects belonging to 7 well characterized families from a larger cohort of over 500 families and 3000 individuals that has been studied in our center in a series of NIH-funded projects. We are currently performing the microarray-based component of our project using the Illumina Infinium 450 Beadchip assay. In the second stage of this project, we will use MBD-seq methodology to study the same subjects. Finally, we will validate our methylation results by assessing DNA methylation in 10 selected genes using Epityper (analysis of DNA methylation using mass spectrometry).

Analysis: The data will be analyzed using SOLAR (Sequential Oligogenic Linkage Analysis Routines) to estimate the genetic and environmental components of DNA methylation profiles and associated phenotypes, and identify genotype-by-age and genotype-by-pubertal stage interactions, using pedigree information and parental phenotypes to estimate hereditary versus environmental components.

Conclusion: We will present our preliminary microarray data at the meeting. After all phases of the project including statistical analysis are completed we expect to be able to assess the pros and cons of both technologies and to plan for large-scale DNA methylation analysis using the NCS cohort.