Evidence for the Transcription Factor Occupancy Theory: An \textit{in silico} Analysis of DNA Methylation Responses to Metal Exposures in Adults

Wednesday, April 13\textsuperscript{th} | MHRC 1304 | 10:00 A.M.

The mechanism by which DNA methylation patterns are orchestrated is still poorly understood. In the context of environmental exposures, it is hypothesized that the presence of transcription factor binding in gene promoter regions affects the outcome of methylation patterning. Here, an in-silico approach was used to test this hypothesis in the context of adult exposure to metals. 334 unique genes from four microarray-based cross-sectional studies were assembled for analysis. Comparison was done on the basis of gene function as well as common transcription factor binding sequences between gene promoter regions. Despite the presence of only two overlapping genes at the gene list level, 43 unique transcription factors were found to be common within gene lists associated with at least one study. Ten of these transcription factors were common across the majority of studies. These results are highly consistent with previous work involving in-utero subjects. Additionally, TFs also show common responsiveness to the Glucocorticoid Receptor pathway, a pathway characteristic of environmental stress response. Together, this study supports the transcription factor occupancy theory as a mediator of environmental epigenetic response.

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