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## DNA Methylation Barriers

In normal differentiated cells, most of the genome is densely methylated, except CpG islands near promoters of actively transcribed genes. Maintaining this boundary between unmethylated promoter-associated and adjacent methylated regions is crucial as loss of segregation can lead to disease. Unfortunately, it is not clear where these boundaries are, what happens to barriers to make the promoters susceptible to methylation, and how these changes progress. Understanding the mechanisms that protect these promoter regions could help in preventing methylation spreading and further the understanding of epigenetic regulation and human diseases.

Researchers at the Biodesign Institute of Arizona State University have developed a computational and experimental method to investigate methylation barriers. They particularly looked at promoter-associated CpG islands juxtaposed with genomic repetitive elements as they may serve as methylation centers, exposing adjacent regions to methylation pressure. Further, they identified a single sequence motif that was enriched in protected segments compared to unprotected segments. This method was used to investigate the methylomes of colorectal cancer and discovered more than 500 methylation barriers sharing this single sequence motif. Gradual loss of protection was associated with progression of colorectal cancers and markers of the CpG island methylator phenotype.

This novel method not only advances epigenetic regulation research, but may also be useful in disease screening/risk assessment and in identifying potential therapeutic targets.

### Potential Applications

- Screening
  - Detecting the absence of a methylation barrier for disease risk
  - Detecting the presence of cancer
- Further understanding of epigenetic regulation
- Could help identify genetic sequences involved in protection against methylation to prevent disease

- Potential drug targets

#### Benefits and Advantages

- First genome-wide scanning of methylation barriers around promoters
- Sequence motif characterizes the local sequence context
- Functional validation of the methylation barrier and fine-mapping strongly support computational predictions
- Depict the landscape of methylation barriers in the human genome
- Advances the understanding of epigenetic regulation and human diseases

For more information about this opportunity, please keep an eye out for this publication in press

Shu et al; Genome-wide screening and functional validation of methylation barriers near promoters. Nucleic Acid Research (2024 in press)

For more information about the inventor(s) and their research, please see

[Dr. Liu's departmental webpage](#)