



Influence of DNA methylation on transcriptional factor binding sites and regulation of transcription

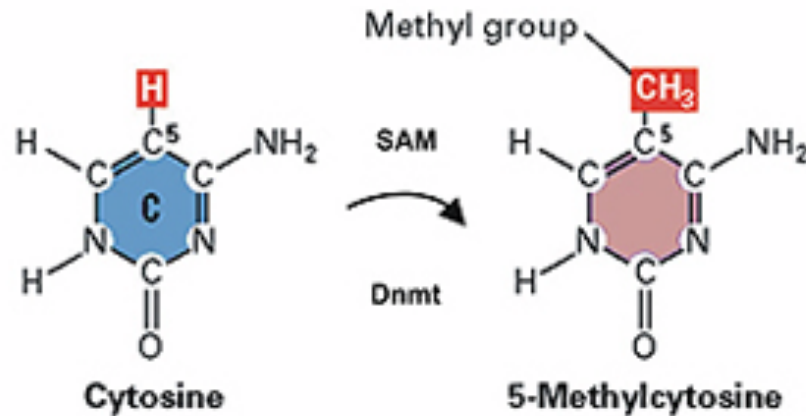
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FANTOM5 consortium

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DNA methylation

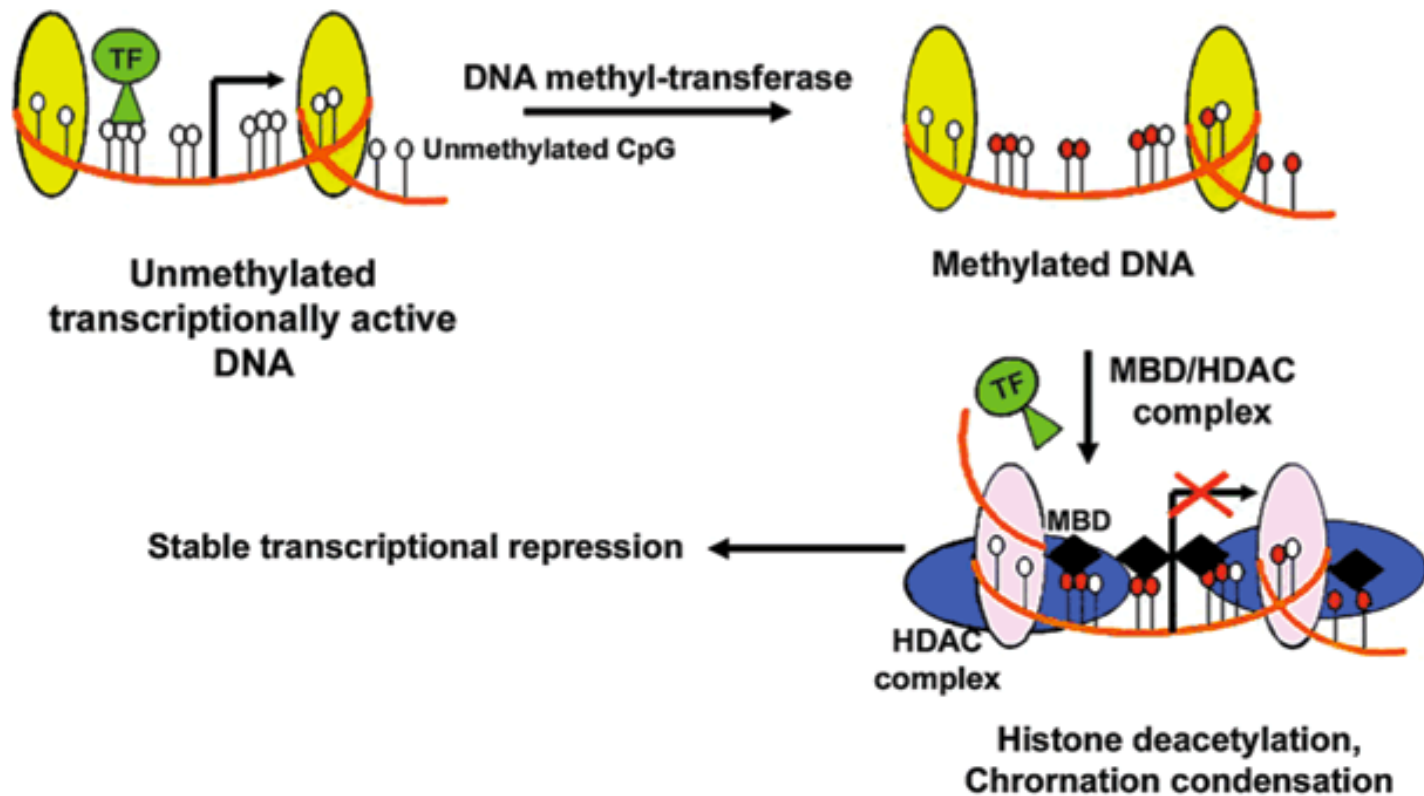


DNA Methylation in Vertebrates



Most often 5mC appears in CG content (but also possible in CHG or CHH content, especially during early development)

DNA methylation and protein binding (hypothesis)



BUT...



There are many examples of methylated
cytosines within active promoters



What transcriptional factors are more prone to influence of DNA methylation?

Differentially methylated cytosines selection



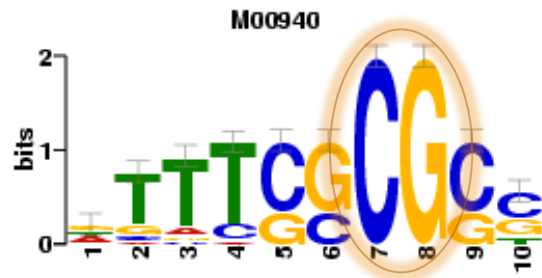
- RRBS (reduced representation bisulfite sequencing) data from Epigenome atlas
- Common samples between Epigenome atlas and FANTOM5
- Cytosines having differentially methylated profile in those samples (<0.2 and >0.8)
- CAGE-tags clusters from common samples having differentially methylated cytosines in $[-800..+200]$ regions
- TFBS (based on RDM) overlapping with DMC

Samples in common (FANTOM5 & Epigenome Atlas)

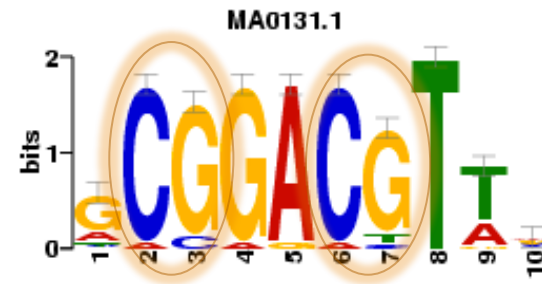


- Fibroblasts
- CD34+
- Pancreatic stromal cells
- Pancreas, adult
- H9 embryonic stem cells
- Skeletal muscle cells
- CD19+, B cells
- Kidney, adult
- Smooth muscle cells
- Brain, fetal
- Heart, fetal
- Lung, fetal

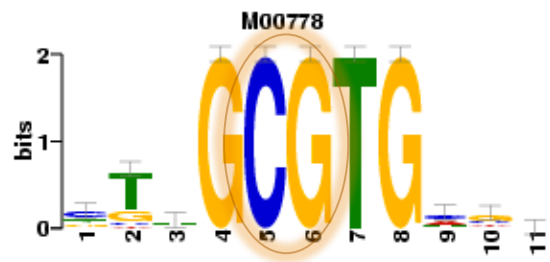
Results: TFs sensitive to DNA methylation contains CG as “strong” TFBS positions



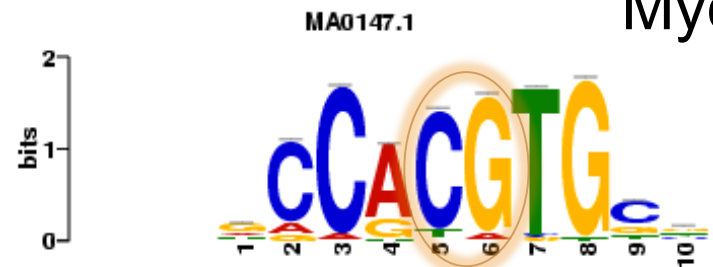
E2F



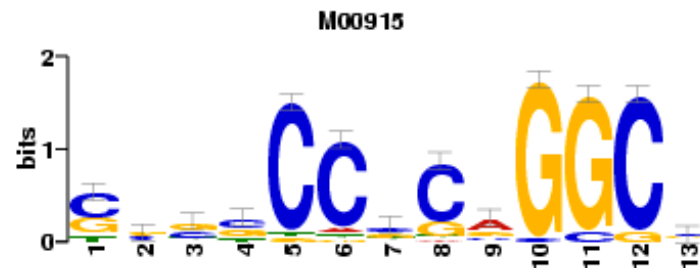
MIZF



AhR



Myc

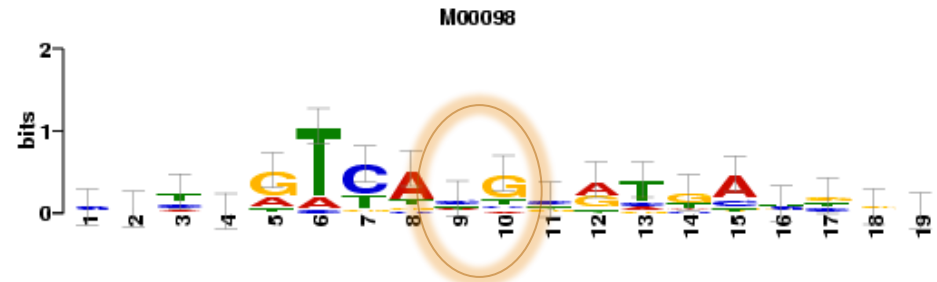


AP2

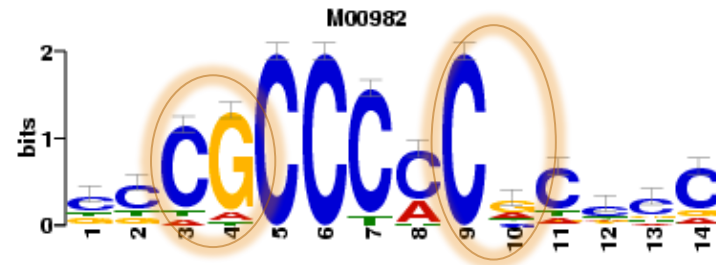
Results: TFs not sensitive to DNA methylation contains CG (C or G) as “weak” positions



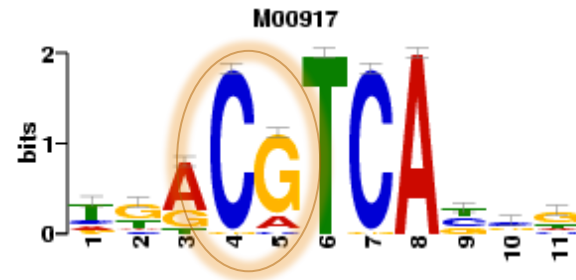
Pax2



KROX, Egr1



CREB



Conclusions



1. Most of TFs are sensitive to DNA methylation of their TFBS.
2. TFs, containing CG as “strong” positions of the TFBS, are more sensitive to DNA methylation comparing to those, having C or G as “weak” positions.



Annotation of CAGE-tags clusters with differentially methylated cytosines can be provided for the FANTOM5 consortium

Thanks



RIKEN OSC team

KAUST team

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FANTOM5 consortium