Andrew Smith

Molecular and Computational Biology section
Division of Biological Sciences
University of Southern California.

Precisely bounding genomic regulatory regions in mammals using high-resolution DNA-methylation data

DNA methylation is unique among epigenomic marks in that it is associated with individual nucleotides, and in mammals almost exclusively at CpG sites. Since the emergence of high-throughput bisulfite sequencing, several full-genome single-CpG methylation profiles, or methylomes, have been produced in human, mouse and chimp. Mammalian genomes are highly methylated almost everywhere, except at hypomethylated regions (HMRs) typically associated with promoters or enhancers. These HMRs can be identified with very high precision to indicate the likely boundaries of regions that are accessible to transcription factor binding. HMR boundaries are highly consistent across methylomes and often identifiable to a single nucleotide position, suggesting a mechanism regulating the boundaries. However, at many tissue-specific genes we observe tissue-specific shifts in HMR boundaries around promoters. Similarly, cases of expanding or contracting HMRs can be found when comparing methylomes between species. We hypothesize that these boundaries indicate precisely where the regulatory elements reside near a gene, and may indicate the extent of the proximal promoter for a given gene. I will discuss the available data, explain how these data are analyzed and describe interesting examples. I will also discuss the implications for our understanding of promoter organization in mammals.