SPRING Meeting

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Keywords: VCSCB SPRING seminars

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Meeting Details

Start Date / Time	February 13, 2019 at 9:00 AM
End Date / Time	February 13, 2019 at 10:00 AM
Duration	1 hour(s)
Location	9455 MRB IV
Presenter Name	Kelly Barnett (Hodges Lab)
Presentation Title	Capturing spatiotemporal dynamics of DNA methylation across the chromatin accessible genome during cell fate specification
Status	This meeting has already occurred

Meeting Agenda/Notes

While DNA methylation (DNAme) patterns are highly dynamic and cell-type specific at enhancers, current models inadequately describe the role of DNAme within the ordered process of enhancer activation and cell differentiation, both frequently perturbed in human disease. DNAme is suggested to be crucial for cell differentiation, as stem and progenitor cells defective for DNAme pathways demonstrate impaired cell differentiation. Previously, we identified a class of non-coding genomic regions among the methylomes of discrete hematopoietic cell types that appear to undergo progressive DNA demethylation across cell fates. Intriguingly, many of these same genomic regions while methylated, exist in nucleosome-depleted genomic regions. This led to a hypothesis that chromatin accessibility (ChrAc) and DNAme dynamics are separate molecular events representing distinct stages of enhancer activation. Thus, we developed a method (ATAC-Me) to probe ChrAc and DNAme from a single DNA library by coupling assay for transposase accessible chromatin (ATAC) with subsequent bisulfite conversion. We have applied ATAC-Me across a THP1 monocyte to macrophage cell differentiation time course. We identified multiple waves of ChrAc changes decoupled from DNAme changes supporting that concomitant ChrAc and DNAme are a unique enhancer activation stage. In contrast, we observed ChrAc dynamics and nearby transcriptional responses remain coupled regardless of intergenic DNAme state. Further, transcription factor (TF) footprints were effectively ascertained from ATAC-Me, and enriched for TF motifs corresponding to distinct ChrAc and gene regulatory responses. Collectively the ATAC-Me methodology offers a new tool to characterize the DNAme and ChrAc relationship in a multitude of contexts. In this work we have applied ATAC-Me to construct a timeline for enhancer activation events, namely, ChrAc and transcriptional dynamics preceding DNAme changes across cell differentiation.

Attachment

Spring_2019_Email_Notice_Barnett.pdf - Added on February 7, 2019 at 3:32 PM by Pam Uttz