DukeNUS Medical School

Signature Seminar Series

Methylation Mesa Define Functional Regulatory Elements for Targeted Gene Activation

ABOUT THE LECTURE

DNA methylation & mRNA expression correlations are often observed with inconsistent evidence supporting causal regulation. We hypothesized that causal regulatory elements exhibit heightened demethylation sensitivity. To identify, we analyzed 19 whole genome bisulfite sequenced samples before & after demethylation & identified narrow width (45-294 bp) elements exhibiting demethylation hypersensitivity within a short plateau, termed Methylation Mesa (MM). The Mesa signature was conserved across species & largely independent of CpG islands. Mesa also demonstrated high concordance with primed / active histone marks. To assess causality, we developed CRISPR-DiR, wherein DNMT1 interacting RNAs (DiRs) were coupled to CRISPR to introduce targeted demethylation with superior resolution. We demonstrated that demethylation of a Mesa triggers locus & distal chromatin rewiring events that initiate mRNA expression significantly greater than promoter CpG island targeting. Thus we report narrow width genome wide regulatory elements capable of initiating gene transcription & provide a fine resolution technology for their targeted and precise demethylation for both validation & therapeutic purposes.

Speaker: **Dr Mahmoud Bassal, Ph.D.**
Bioinformatician
Instructor in Medicine
Harvard Medical School



Host: **Dr Enrico Petretto**
Associate Professor & Director
Centre for Computational Biology
Duke-NUS Medical School

Date: **Tuesday, 18 June 2024**

Time: **12.00 PM - 1.00 PM**
(Light refreshments will be served at 11.30 AM)

Venue: **Duke-NUS Medical School**
Amphitheatre, Level 2

Contact Person: **Ms Kathleen Chan (kathleen.chan@duke-nus.edu.sg)**
Duke-NUS Research Affairs Department

ABOUT THE SPEAKER

Dr Bassal has a distinctive background in both dry and wet-lab research. His research centers on unraveling the interplay between dysregulated metabolism and epigenetics in cancer, specifically investigating how these factors contribute to disease initiation and progression. Dr. Bassal also specializes in custom computational analyses. His bespoke pipelines address complex biological questions, while his work on tools like ChIP-AP and the upcoming CARAS, promise to empower researchers worldwide.

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