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A transcriptional memory model for the Epithelial to Mesenchymal Transition

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Keywords: Epigenetics, Transcription, Epithelial to Mesenchymal Transition

Cells respond and adapt to environmental stimuli by stably retaining epigenetic marks of prior transcriptional activation, altering cellular responses to the same stimulus when encountered in the future. We developed a cell culture model to study this transcriptional memory during the epithelial to mesenchymal transition (EMT), a cell state change central to both development and disease states. To do this, we used an epithelial mouse mammary gland cell line that reversibly undergoes EMT in response to transforming growth factor beta (TGFβ). We show that TGFβ stimulation establishes transcriptional memory, leading to altered transcriptional responses of a subset of genes upon re-stimulation. In our model, the memory response was inherited through ∼22 cell divisions and led to increased migratory capacity upon re-stimulation with TGFβ. We performed genome-wide characterization of this model, including histone modifications (CUT&RUN), nascent RNA (PRO-seq), chromatin accessibility (ATAC-seq) and DNA methylation analyses (Nanopore). We found that the memory response was selective, as only 25% of all TGFβ responsive genes demonstrate an elevated response, while another 25% shows a refractory response, to re-stimulation. Mechanistically, DNA methylation, cell signaling, and paused Pol II do not appear to play a role in establishing this transcriptional memory. However, we found that enhancer histone modifications H3K4Me1 and H3K27Ac bookmark the TGF-β primed genes and enhancer elements. Our data suggest that enhancer-promoter contacts might be involved in establishing and retaining the transcriptional memory response.

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Abstract 1885

Surveillance of Pathogens in Aquatic Environments

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Keywords: metagenomics, fresh water, pathogens

Twenty percent (20%) of annual deaths worldwide are attributed to microbial pathogens. Pathogenic illnesses pose major threats to the overall health and safety of humans. These illnesses can result in death, prolonged hospital stays, and increased hospital expenses. The goal of this research is to study the evolution and ecology of microorganisms and surveillance of human pathogens in local the ponds. Surveillance of pathogens can inform the local and global efforts for monitoring and supporting public health measures to fight diseases. Surveillance is the essential tool to inform policies, prevent infections and control responses. Samples were collected from four ponds in Jackson, TN: Lane College, Muse Park, Fairgrounds and Campbell Street Park. DNA was isolated from the water samples using ethanol precipitation followed by the ZymoBIOMICS DNA Miniprep kit. Samples were prepared for the whole genome sequencing by PCR using the Rapid Barcoding and the 16S PCR Barcoding kits from Nanopore to amplify the DNA samples. The metagenomic DNA was sequenced with the Nanopore M1KC MinION sequencer. The reads were then analyzed by the Epi2Me, What's in my pot (WIMP) or 16S Fastq workflows. All four of the ponds are known to have pathogenic in them. The Lane College Pond has Clostridium and Pseudomonas. The Fairgrounds Pond has Bacillus and Legionella. The Campbell Street Pond has Clostridium, Bacillus, Leptospira and Pseudomonas. The Muse Park Pond has Leptospira, Legionella, and Clostridium. Further studies can be done with this project to examine the concept of how pathogens affect microbiomes in an aquatic environment.

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