Research Strategy

Significance:

. The existing dogma states that there is a closing of the genome as cells become differentiated into terminal cells from progenitors. How these different epigenetic landscapes are formed during differentiation is a central question of biology. The process of hematopoiesis allows us to study the change in epigenetics as progenitor cells differentiate into terminal cell types. The genome is wrapped out histones into discrete packages called nucleosomes, and the proteins of these histones can be marked with certain modifications that allow regulation of gene expression. However, genes cannot be transcribed while wrapped in nucleosomes, and so the DNA code must be unwrapped and made accessible before transcription can occur. ATAC-seq allows us to find unwrapped sections of DNA, and we can measure the accessibility of DNA during differentiation in sections of the genome that are marked by histone modifications. We can measure at which step in the differentiation process that these common sections of marked chromatin become accessible, and through motif analysis we can identify which transcription factors are the initial factors that are present during these crucial differentiation stages.

The simplest metaphor for the genome is the computer code that encodes every possible cell function. All cells in the body share the same genetic code, yet different cell types with specific functions exist in different environments. Genes are differentially regulated in different tissue types by the way in which the code is read. Several mechanisms regulate the parts of the code that are available to be read and how they are read. These mechanisms exist as part of the epigenome. How these different epigenetic landscapes are formed during differentiation is a central question of biology. Transcription factors bind to certain motifs in the genome and recruit protein complexes that start the process of transcription. However, genes cannot be transcribed while wrapped in nucleosomes, and so the DNA code must be unwrapped and made accessible before transcription can occur. ATAC-seq allows us to find unwrapped sections of DNA, and we can measure the accessibility of DNA during differentiation in sections of the genome that are marked by histone modifications. We can measure at which step in the differentiation process that these common sections of marked chromatin become accessible, and through motif analysis we can identify which transcription factors are the initial factors that are present during these crucial differentiation stages.Hematopoiesis is a unique feature that is a fertile ground for the study of development and gene regulation.

Cell differentiation requires progenitor cells to be “silenced” but “poised” and ready to differentiate into a diverse set of terminal cells possessing distinct functions.