Detecting Differential Transcription Factor Binding Using Single-Cell Sequencing

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Common genetic diseases—systemic diseases caused by thousands of mutations—affect millions of people around the world. Many of these mutations fall within regulatory regions. While the mutations associated with these diseases are widely known, the link between these mutations and their role in disease pathogenicity has largely gone undiscovered, serving as the premise for this project. Single-cell ATAC sequencing, which examines cells at individual levels (rather than in bulk), provides a venue in understanding the biological effect of mutations on cells. This study aims to harness this novel technology to distinguish bound and unbound transcription factors, which play a pivotal role in gene expression. We hypothesized that bound transcription factors would have fewer lower accessibility or ability for sequencing enzymes to cut into the region. Using data from CD8+ T-cells, relevant transcription factors were identified based on enrichment. Expected and observed cuts were computed for each relevant transcription factor site. Potential bound and unbound sequencing sites were identified after calculating the significance between the observed and expected. Finally, a base-by-base metaplot was developed for bound and unbound transcription factor sites to examine differences between the two. In the end, the study finds that regions with lower observed cuts than expected cuts conferred protection from sequencing enzymes, indicating the presence of a bound transcription factor. In distinguishing between bound and unbound transcription factors, the study paves the way for using single-cell ATAC-seq to understand the biochemical mechanism underlying common diseases by identifying the cell types and changes in transcription factor binding caused by genetic diseases.

Awards Won:

Second Award of $2,000

China Association for Science and Technology (CAST): Award of $1,200

American Committee for the Weizmann Institute of Science: Alternate for trip