

Single-cell Multi-omics analysis reveals Gene Regulatory Network at Single-cell Level during Early Stage of Direct Cardiac Reprogramming

Bella Qian

The high global incidence of heart diseases drives the interest in cardiomyocytes regeneration. Specifically, the direct conversion of cardiac fibroblast to induced cardiomyocytes (iCM) holds great promises in regenerative medicine. Direct reprogramming of cardiac fibroblast into induced cardiomyocytes can be achieved by forced expression of cardiac transcription factors, such as Mef2c, Gata4, and Tbx5 (a transcription factor combination referred to as MGT)^{1–3}. To identify how the upstream chromatin landscape drives the transcriptome remodeling process during cardiac direct reprogramming, we performed a parallel single-cell assay for Transposase-Accessible Chromatin using sequencing (scATAC-seq) and single-cell RNA-seq (scRNA-seq) on early reprogramming iCMs as the known epigenetic changes begin on day 3. Many cardiac reprogramming studies have been focusing on the identification of transcriptional factors (TF) to enhance the direct reprogramming process using integrating scRNA-seq and scATAC-seq dataset^{4–6}. However, profiling different cell modalities by computational integration method may not fully capture the true biological state⁷. Compared to integrated data, multi-omics data simultaneously profile multiple data types in the same cell, which deliver more accurate information on molecular process underlying a cell's physiology^{7–9}. My study uses the latest single-cell multi-omics data to unravel the underlying mechanism of cardiac direct reprogramming. In this study, making use of the multi-omics dataset sequenced on the same sample, we determined the matching efficiency of integrative analysis by comparing the number of DORCs between the computationally integrated and multi-omics datasets. Furthermore, with motif analysis, we identified the TFs responsible for the chromatin accessibility dynamics of DORCs during cardiac reprogramming.

<https://symposium.foragerone.com/2022-unc-ch-celebration-undergraduate-research/presentations/41475>