Investigating Epigenetic Modifications in Chromosome Structure in Cardiomyocyte Differentiation Mechanisms for Heart Disease Treatment

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Cardiovascular diseases are the most common cause of death in the world. Because humans form few cardiomyocytes post-birth, engineering new myocardium could transform the treatment of heart diseases. Currently genetic engineering focuses on RNA expression, which overlooks noncoding DNA and has difficulty in distinguishing cell types in early development, such as left and right ventricular cells. This project investigated whether scRNA-seq (transcriptomic) data combined with scATAC-seq (epigenetic) data can be used to differentiate LV, RV, LA, and RA cardiomyocytes to locate novel cis-regulatory elements in the human genome. scATAC-seq data measures chromatin accessibility, a heritable epigenetic modification. Importantly, scATAC-seq can locate novel noncoding regulatory sequences (DNA that does not code for proteins), a sparsely studied portion of DNA sequences in developmental cardiology. scATAC-seq and scRNA-seq data from roughly ~800,000 anatomically informed mouse embryonic cardiac cells were downloaded. scRNA-seq analysis allowed for the annotation of each cell by chamber type and scATAC-seq peak analysis was then performed to analyze statistically significant differential chromatin accessibility. All data was anonymized and downloaded from publications by external research groups. ATAC-seq analysis successfully distinguished the heart's 4 major chambers. It uncovered differential chromatin accessibility for novel promoter and enhancer sequences as well as in known chamber marker genes, supporting ATAC as a valid cell differentiation analysis metric. These new marker sequences can distinguish the chamber identity of cells in culture derived from induced pluripotent stem cells, enabling scientists to advance stem cell research and regenerative therapies.

Awards Won:
Second Award of $2,000