Unraveling the Impact of Long Terminal Repeats(LTRs) on clonal variation in iPSC Differentiation Efficiency

Induced pluripotent stem cells (iPSCs) are considered a revolutionary breakthrough in understanding disease mechanisms, developing cell therapies, conducting drug testing, and other applications, due to their unique potential to differentiate into various cell lineages in unlimited quantities. However, the complex gene regulatory networks that govern the differentiation rate and proliferation capacity of iPSCs still pose challenges. To understand this complex network, Long Terminal Repeats (LTRs), known as retroviral elements that act as enhancers and promoters, are suggested as potential factors in regulating stem cell gene expression.

We generated cardiomyocytes from two subclones originating from human iPSCs to evaluate the efficiency of differentiation. Cardiac Troponin T (cTnT) was chosen as a marker of cardiac differentiation, along with morphology and beating properties. RNA-Seq and ATAC-Seq were applied to investigate whether LTRs were involved in the differentiation process. The results showed varying expression of known differentiation-related marker genes such as NANOG, MYC, and PRDM14. These findings suggest that LTRs may play a role in regulating stem cell gene expression and contribute to stem cell heterogeneity. Further research is required to fully understand the mechanisms by which LTRs regulate gene expression and how they contribute to stem cell heterogeneity