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TENET+: a tool for reconstructing gene networks by integrating single cell expression and chromatin accessibility data

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Reconstruction of gene regulatory networks (GRNs) is a powerful approach to capture a prioritized gene set controlling cellular processes. In our previous study, we developed TENET a GRN reconstructor from single cell RNA sequencing (scRNAseq). TENET has a superior capability to identify key regulators compared with other algorithms. However, accurate inference of gene regulation is still challenging. Here, we suggest an integrative strategy called TENET+ by combining single cell transcriptome and chromatin accessibility data. TENET+ predicts target genes and regions associated with transcription factors (TFs) and links the target regions to their corresponding target gene. As a result, TENET+ can infer regulatory triplets of TF, target gene, and enhancer. By applying TENET+ to a paired scRNAseq and scATACseq dataset of human peripheral blood mononuclear cells, we found critical regulators and their epigenetic regulations for the differentiations of CD4 T cells, CD8 T cells, B cells and monocytes. Interestingly, not only did TENET+ predict several top regulators of each cell type which were not predicted by the motif-based tool SCENIC, but we also found that TENET+ outperformed SCENIC in prioritizing critical regulators by using a cell type associated gene list. Furthermore, utilizing and modeling regulatory triplets, we can infer a comprehensive epigenetic GRN. In sum, TENET+ is a tool predicting epigenetic gene regulatory programs for various types of datasets in an unbiased way, suggesting that novel epigenetic regulations can be identified by TENET+.

Github page: https://github.com/hg0426/TENETPLUS.