



10X Genomics Multiome(scRNA/scATAC-seq) Introduction

Some advantages/incentives to perform a multiome project

- Allows to refine gene expression data, for instance by identifying subpopulations where a TF is not only expressed but also active (by assessing openness of its target motif sites). Loupe browser allows to look for differential enrichment of TF motifs in peaks of different clusters.
- Identify cell-type specific regulatory regions (correlating and anti-correlating with expression), for instance as described here by 10XG below. This can be done in Loupe Browser. This can help building gene-regulatory networks.

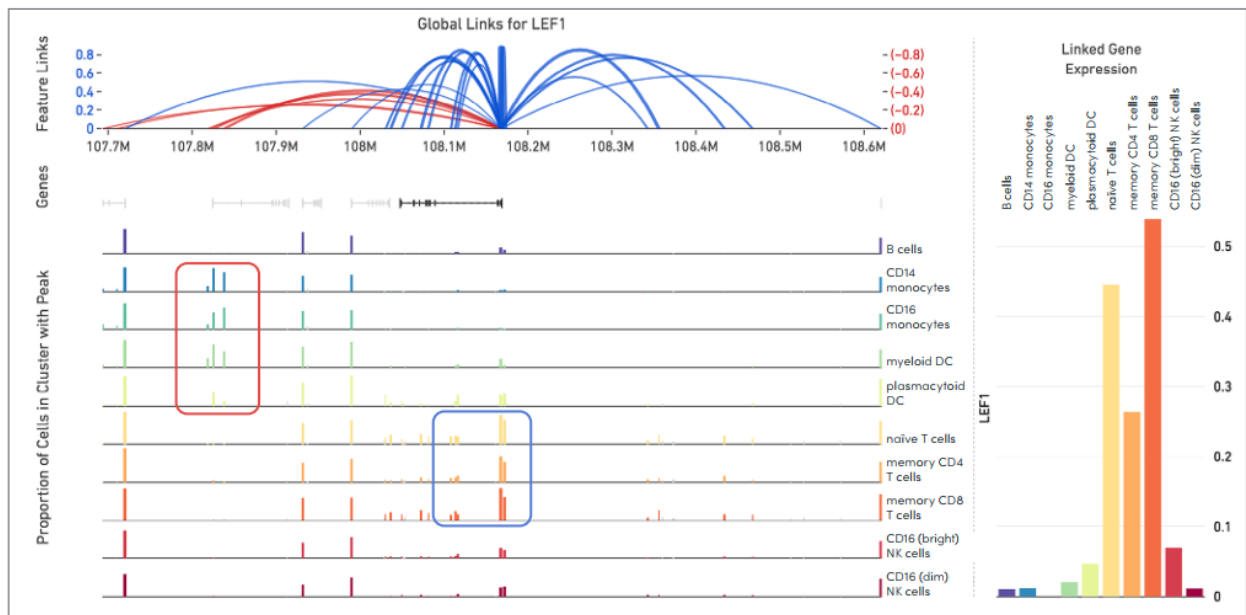


Figure 3. Identification of putative regulatory elements directly linked to a gene of interest. Global links for *LEF1* indicate open chromatin peaks that are either correlated (blue arcs) or anti-correlated (red arcs) with *LEF1* gene expression across a 1 Mb window for the same 7,273 PBMC nuclei seen in Figure 1. *LEF1* expression levels and open chromatin peaks are color coded by cell type. Cell-type specific expression of *LEF1* is correlated with linked open chromatin regions near the *LEF1* promoter that are enriched specifically in naive and memory T cells (blue box). Cells with low *LEF1* expression, such as monocytes and myeloid dendritic cells, each have an open chromatin region several hundred kilobases away that may be repressive (red box).

- Can give hints on gene expression levels of genes whose mRNA are too lowly expressed to be detected by scRNA-seq.
- May improve separation/resolution of clusters.
- Gives hints on future developmental trajectories that are not yet visible at RNA levels.

Some potential pitfalls (non exhaustive)

- The sensitivity of scATAC-seq is intrinsically low, as for each locus only 2 molecules are physically present (one per chromosome). Due to this low sensitivity, scATAC-seq is more amenable to family-wide motif studies (for instance all target genes of factor X rather than an individual target gene).
- ATAC and GEX sensitivities are now better for standalone scATAC v2 and standalone GEX v4 respectively as compared to multiome, which is still based on older versions of these methods. In addition, if cells instead of nuclei are an option for your stand-alone scRNA-seq, more data would be



intro vA.02

retrieved than with multiome, since multiome can only be performed on nuclei.

Versions log

- v1.01: initial release
- vA.02: Some minor changes. Mentioned that multiome is still based on older ATAC/GEX methods. Mentioned that many downstream analyses can be done in Loupe Browser directly.