10X Genomics Multiome (3'scRNA-seq/scATAC-seq) Introduction

Some advantages/incentives to perform a multiome project

- Allows to refine gene expression data, for instance by identifying subpopulations were a TF is not only expressed but also active (by assessing openness of its target motif sites).

- Identify cell-type specific regulatory regions (correlating and anti-correlating with expression), for instance as described here by 10XG below. This can help building gene-regulatory networks.

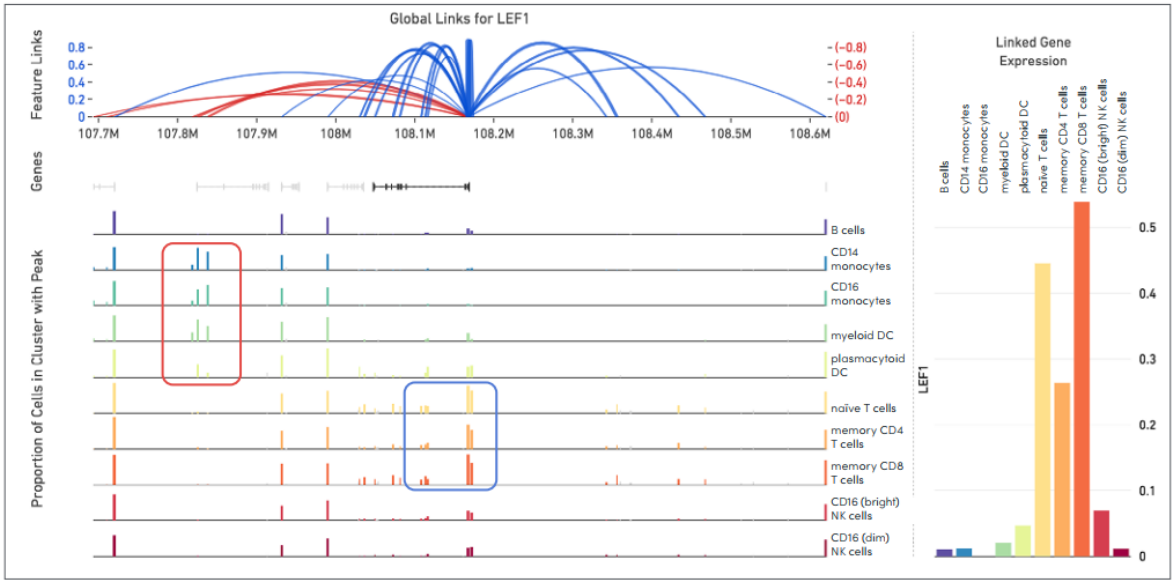

Figure 3. Identification of putative regulatory elements directly linked to a gene of interest. Global links for *LEF1* indicate open chromatin peaks that are either correlated (blue arcs) or anti-correlated (red arcs) with *LEF1* gene expression across a 1 Mb window for the same 7,273 PBMC nuclei seen 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 naïve 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 gives 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.

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).

- Sensitivity is similar between 10XG multiome and stand-alone scATAC-seq (as of v1.1 and v1.0 reagents respectively). For 3'scRNA-seq, it is also similar when comparing to stand-alone 3'scRNA-seq v3.1 done on nuclei. Nevertheless, if cells instead of nuclei are an option for your stand-alone scRNA-seq, more data would be retrieved than with multiome since multiome can only be performed on nuclei.

Versions log

– v1.01: initial release