

# Early epigenetic modulation guides the differentiation of monocytes into macrophages

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## Introduction

- Monocytes are recruited to tissues to participate in tissue repair and inflammation.
- Monocytes differentiate into macrophages upon tissue entry.
- This process is studied using THP-1 cells treated for >48 hour of PMA.

**Aim:** To investigate changes in chromatin accessibility during early monocyte-to-macrophage differentiation using THP-1 treated with PMA for 24 hours cells as a model.

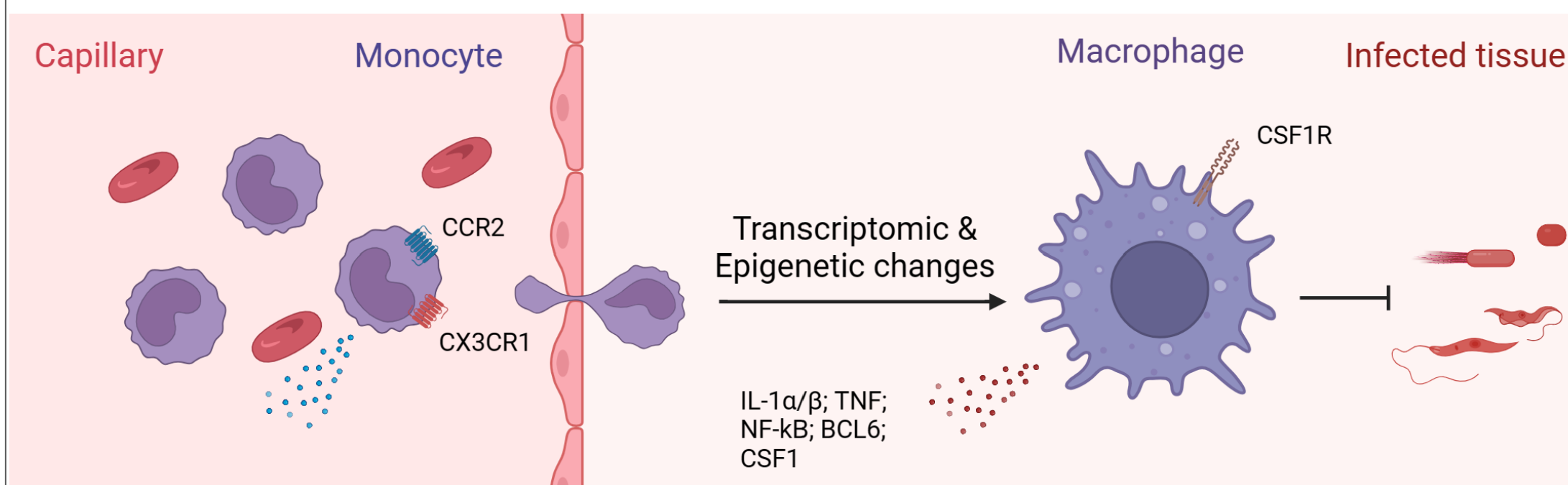


Figure 1. Graphical representation of monocyte-to-macrophage differentiation.

## Methods

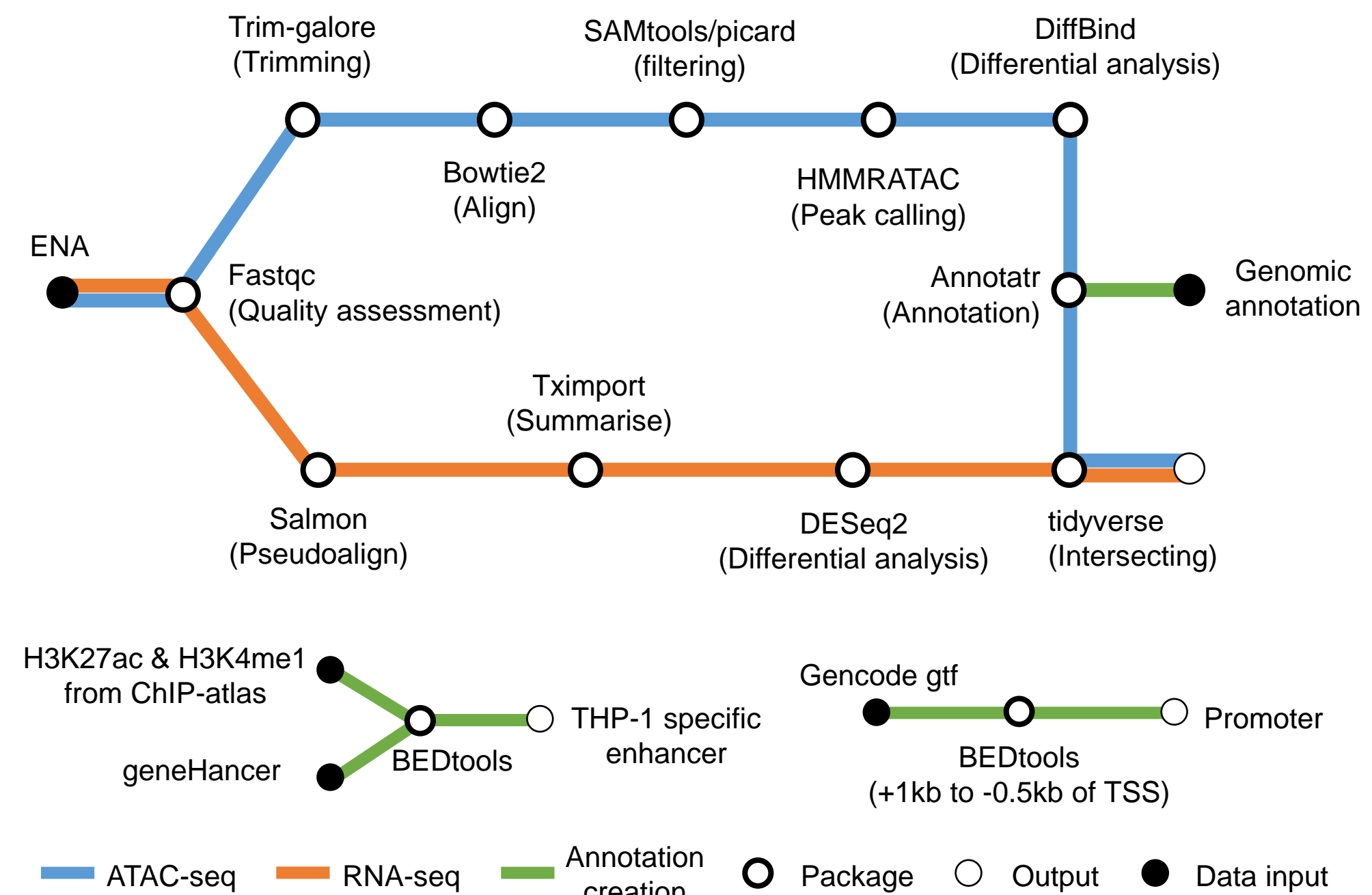


Figure 2. Schematic representation of the analysis pipeline employed.

## Results

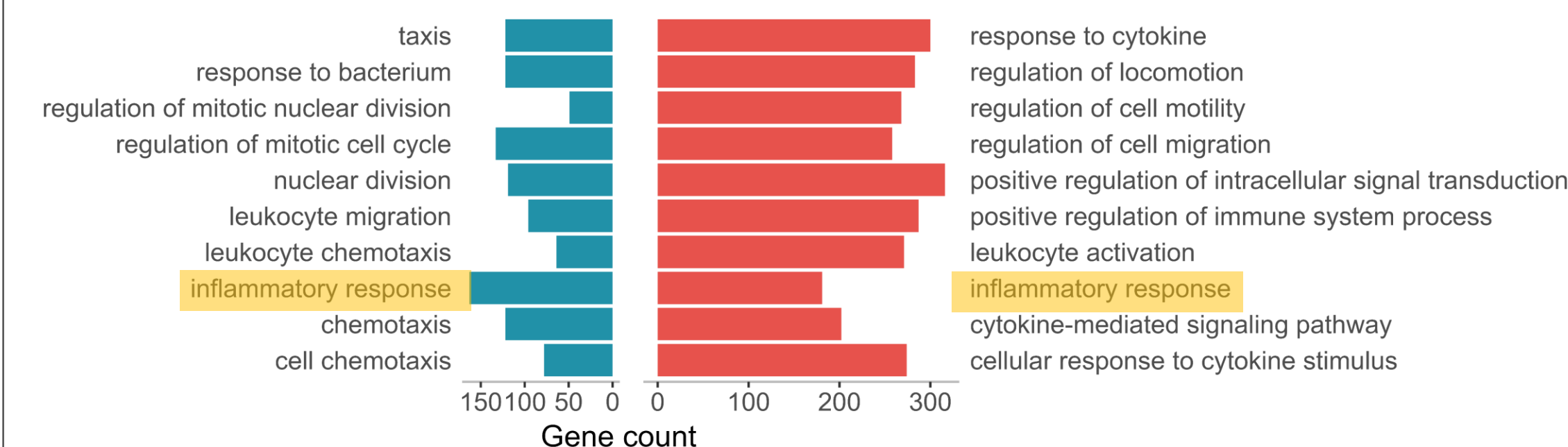


Figure 3. Biological processes over-represented in differentially expressed genes (blue) and differentially accessible chromatin regions (red) following 24-hour PMA treatment of THP-1 cells. Differentially accessible chromatin regions were annotated based on the distance to nearby genes identified using GREAT v4.0.4.

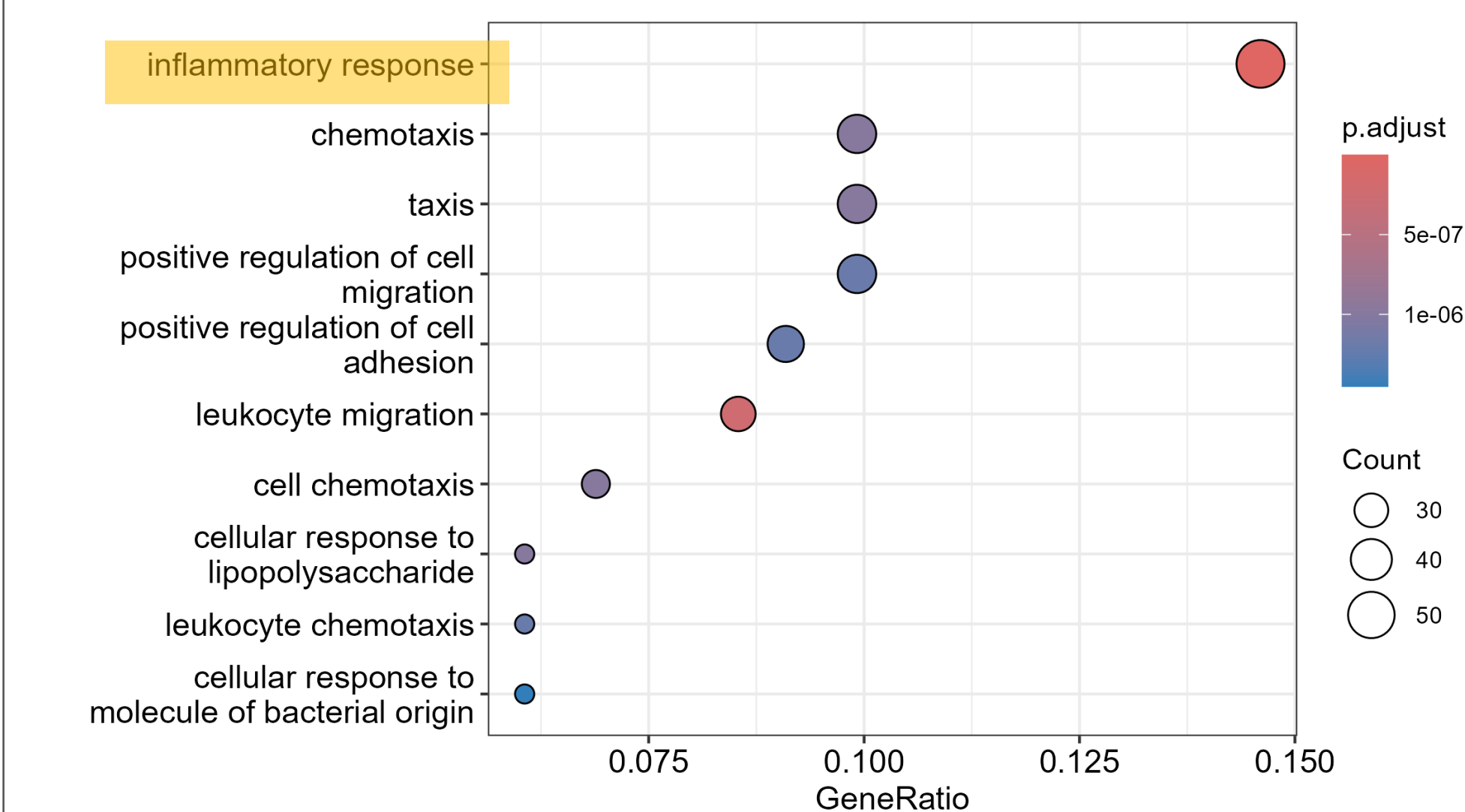


Figure 4. Biological processes over-represented in differentially expressed genes associated with differentially accessible promoter and/or cell type-specific enhancer regions following 24-hour PMA treatment THP-1 cells. Overlap between differentially accessible regions and promoters and enhancers was identified using BEDtools v2.27.0

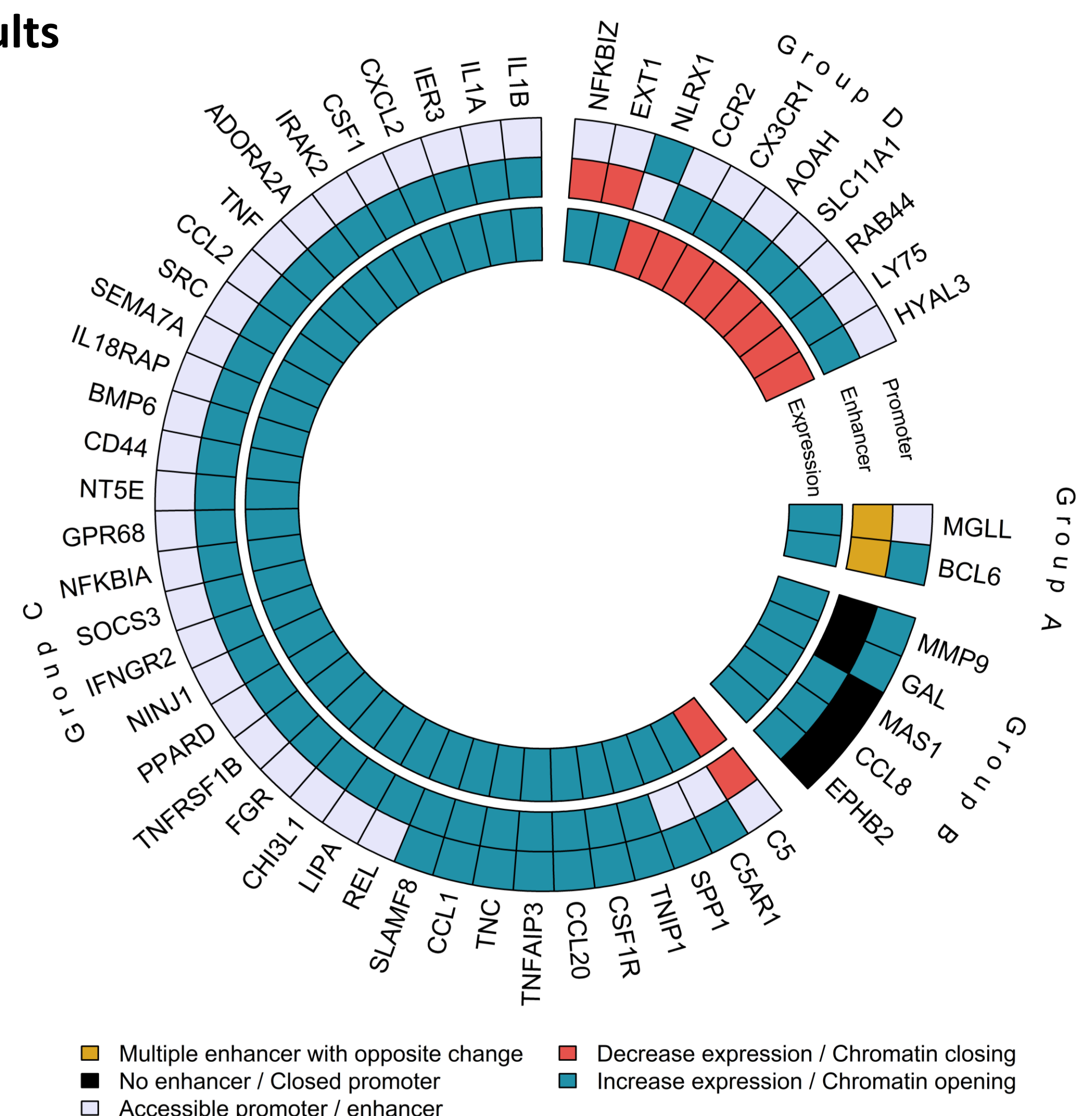


Figure 5. Changes in gene expression are associated with changes chromatin accessibility in genes involved in inflammatory response. Most of the expression response pattern is positively associated with the chromatin accessibility changes in proposed regulatory elements.

## Concluding Remarks

- Changes in both gene expression and chromatin accessibility in THP-1 cells treated with PMA for 24 hours correlate with characteristic changes associated with monocyte-to-macrophage differentiation.
- These changes in gene expression and chromatin accessibility are strongly associated with the inflammatory response.
- These changes are pronounced at genes crucial for driving monocyte-to-macrophage differentiation, including CSF1, CSF1R and IL1A/B.
- Therefore, changes in the expression of genes critical to monocyte-to-macrophage differentiation are likely driven by changes in chromatin accessibility within their promoter and enhancer regions.

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Liu, T., Huang, T., Li, J., et al. (2023) Optimization of differentiation and transcriptomic profile of THP-1 cells into macrophage by PMA. *PLOS ONE*, 18 (7): e0286056. doi:10.1371/journal.pone.0286056.

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