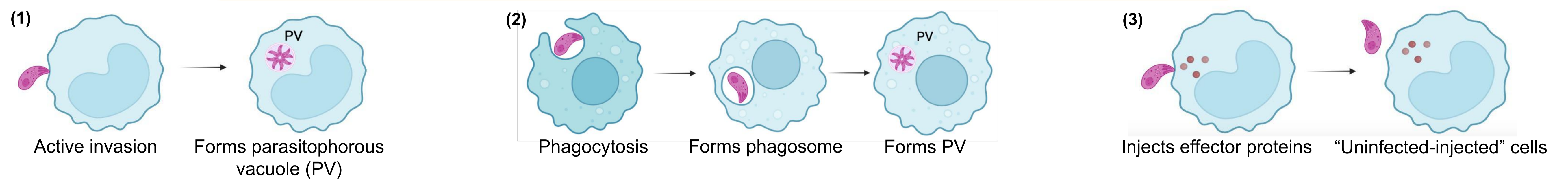


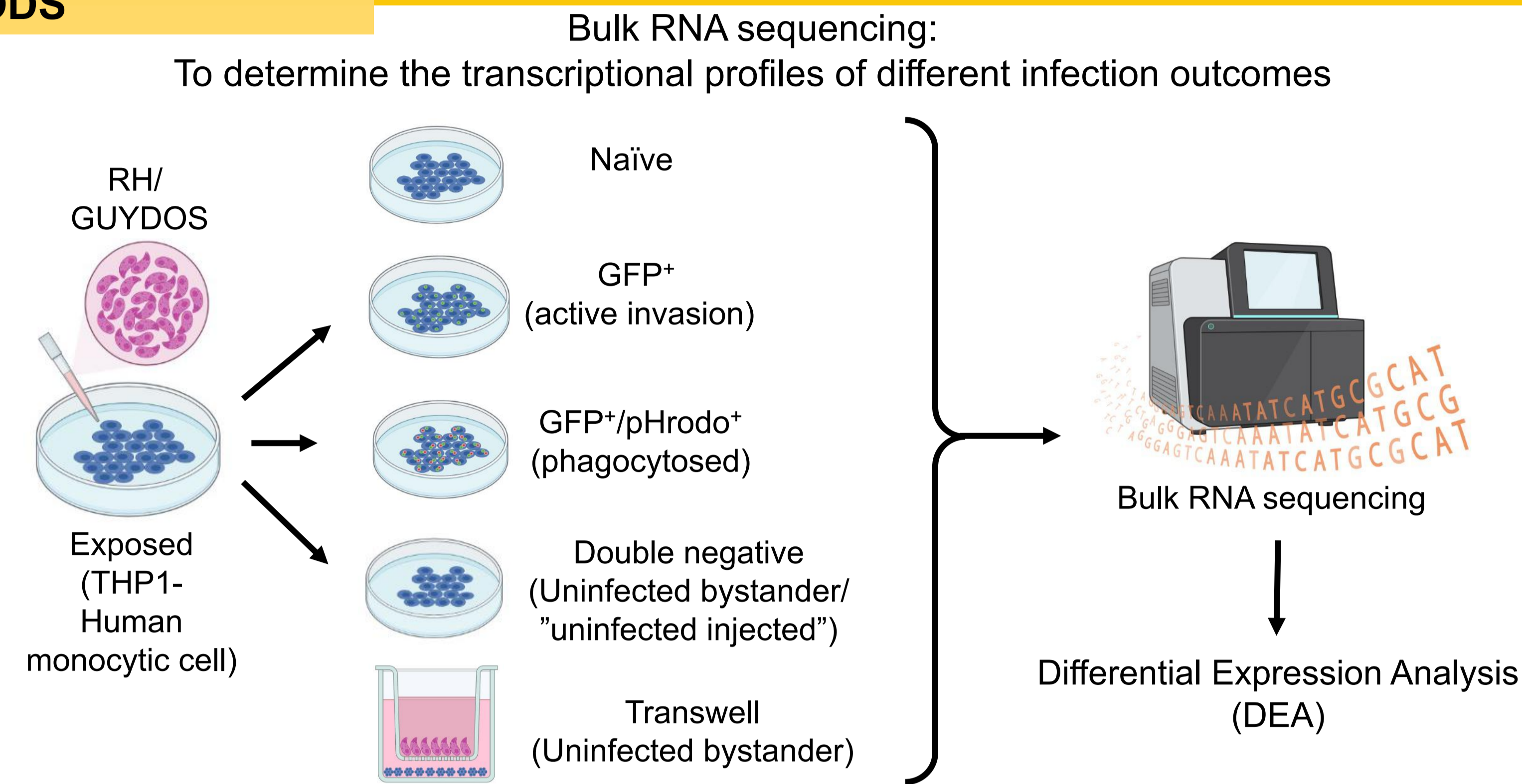
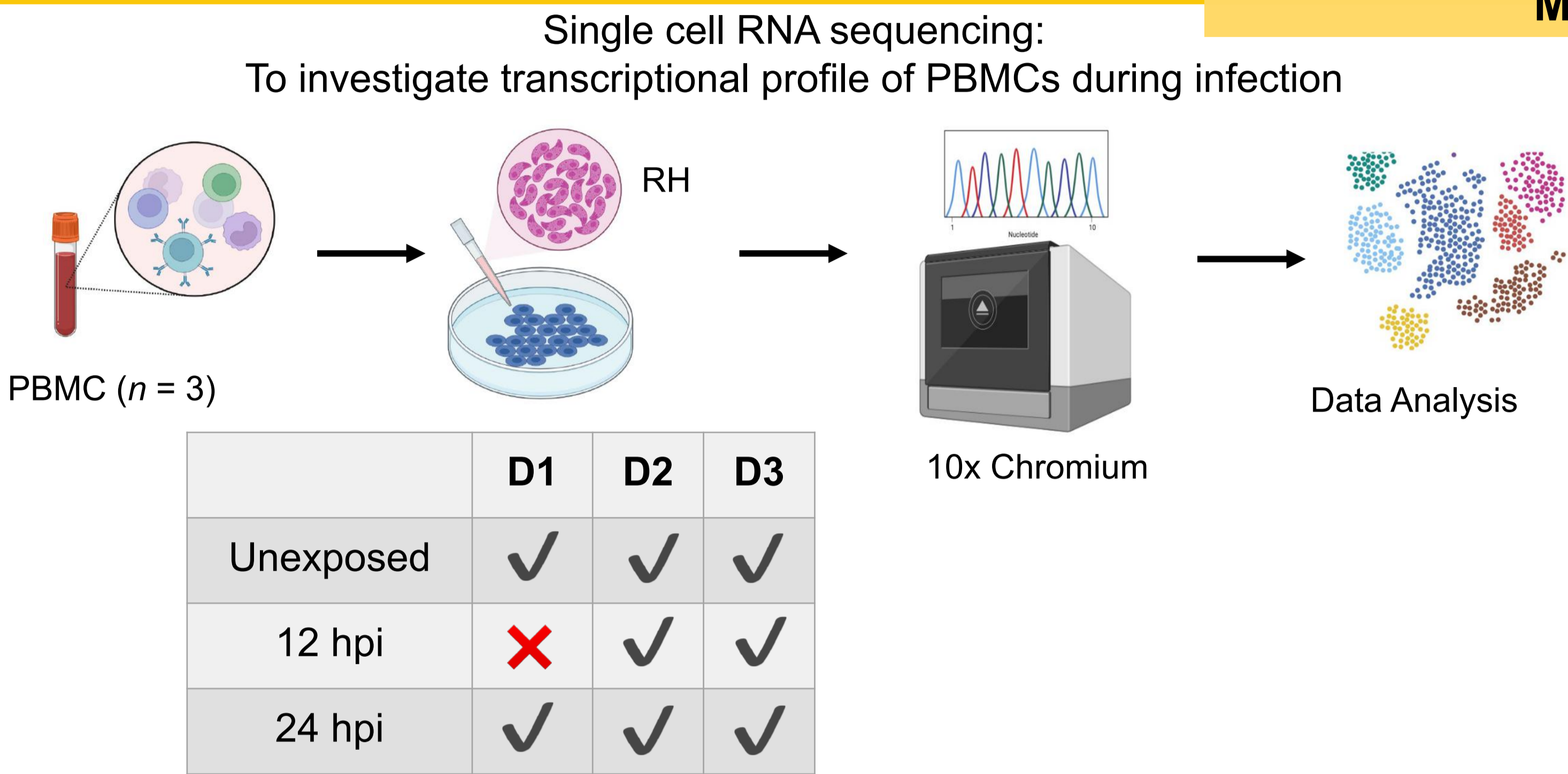
## INTRODUCTION

- Pathogen interaction with host immune cells often result in different outcomes.
- Hence, it is important to understand host-pathogen interaction at a single cell level.
- *Toxoplasma gondii* can simultaneously produce distinct infection outcomes in the same host<sup>1-2</sup>.



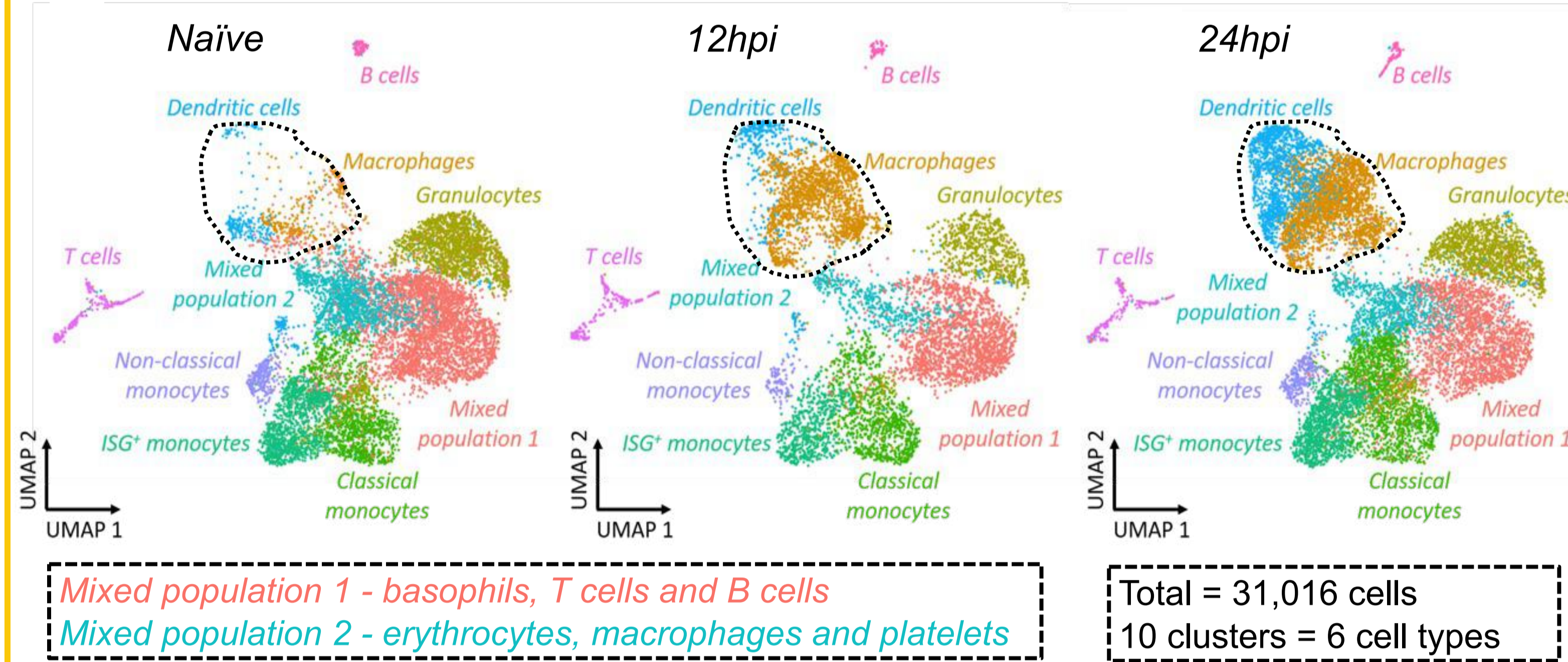
**Aim: To investigate the transcriptional programs that underpin heterogeneous *Toxoplasma*-human peripheral blood mononuclear cells (PBMCs) using a combination of dual single cell and bulk RNA sequencing**

## METHODS



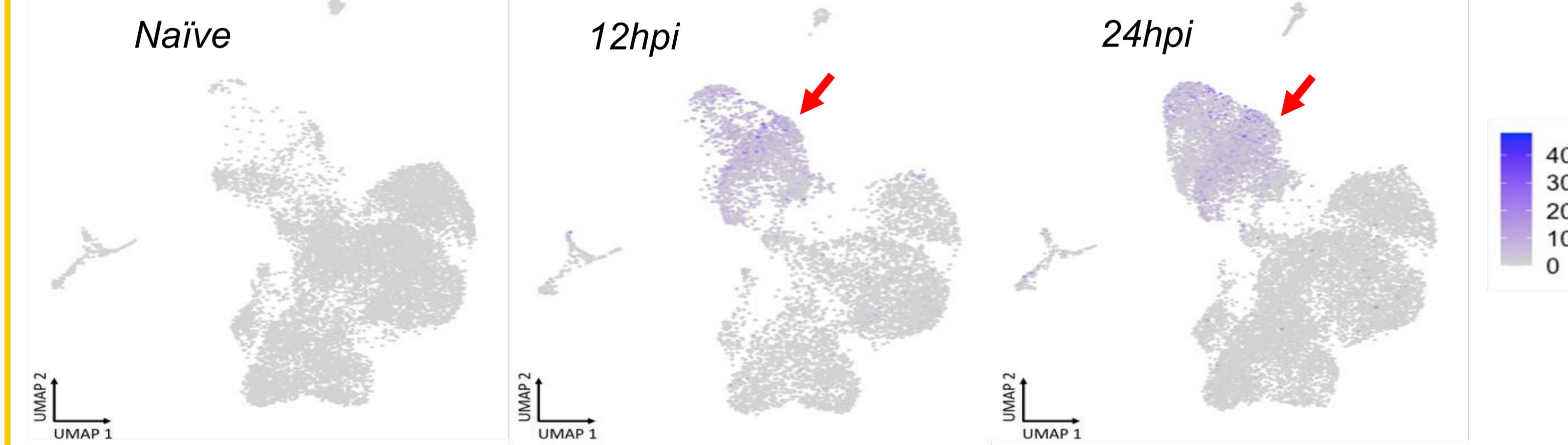
### 1) Differential cell distributions in unexposed and *Toxoplasma* infected PBMCs

(A) scRNA-seq – human PBMCs



- Dendritic cells and macrophages are major cells that transcriptionally respond to *Toxoplasma* infection.

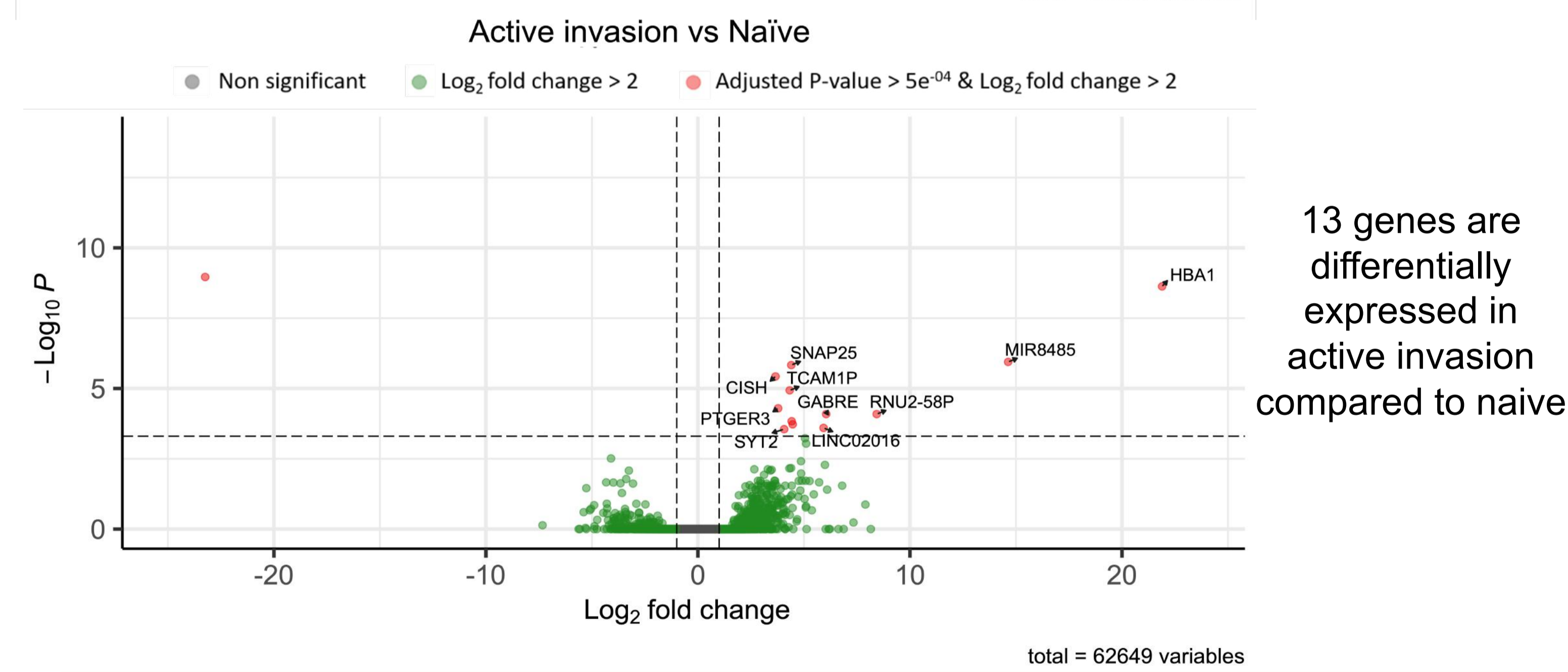
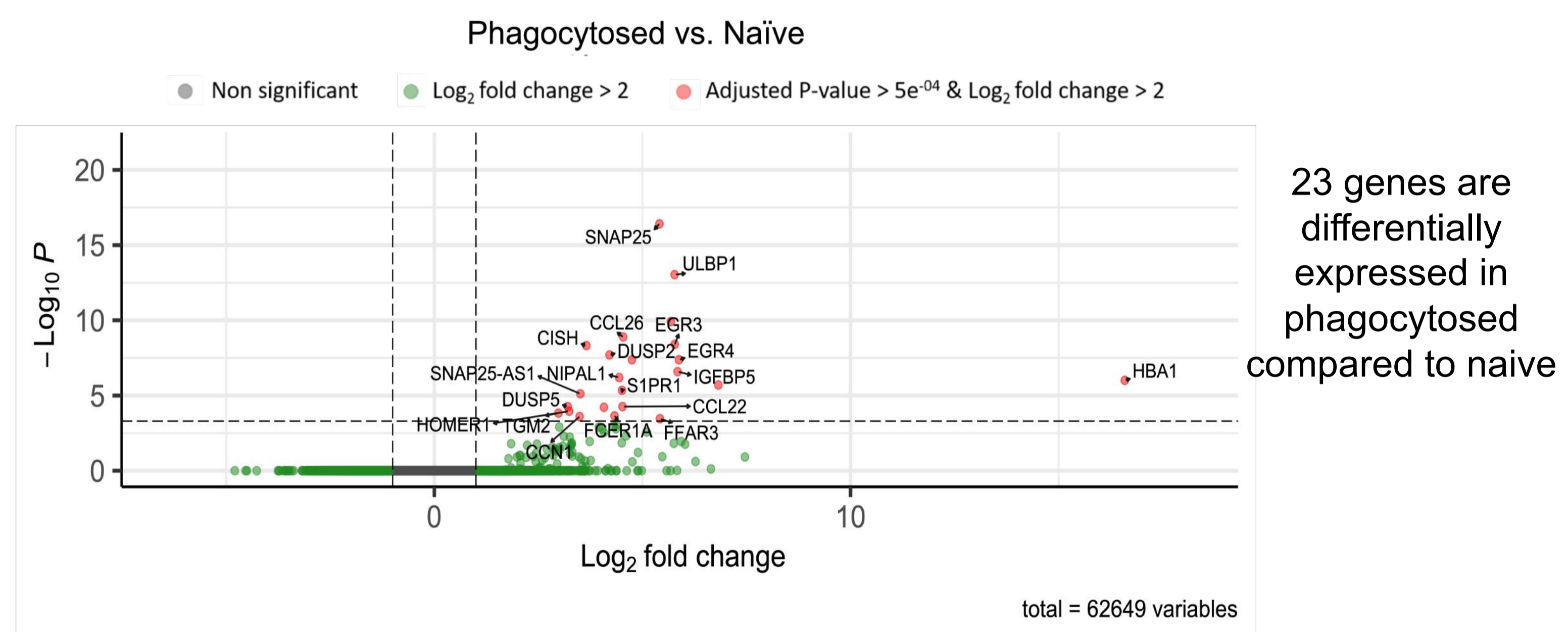
(B) *Toxoplasma* gene expression



- *Toxoplasma* genes highly expressed in dendritic cells and macrophages in infected samples

### 2) Transcriptional heterogeneity in *Toxoplasma*-exposed human monocytic cells

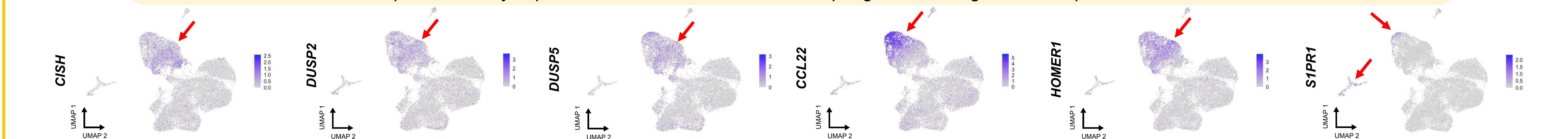
- From DEA, only phagocytosed and actively invaded samples had significantly different transcriptional profile compared to naive.



- These differentially expressed genes could be potential markers to identify *Toxoplasma*-infected cells via phagocytosis and active invasion

### 3) Over representation of differentially expressed genes (DEGs) in phagocytosed sample in dendritic cells and macrophage

- To investigate if the cells were infected either via active invasion or phagocytosis, the expression of DEGs was analysed in the scRNA-seq dataset.
- None of the active invasion specific DEGs detected in the scRNA-seq dataset.
- Five out of 23 DEGs are predominantly expressed in dendritic cells and macrophages and one gene was expressed in T cell cluster.



## DISCUSSION

- *CCL22* expression is induced in phagocytes by *Toxoplasma* to promote growth and dissemination<sup>3</sup>.
- *CISH*, *DUSP2/5* and *S1PR1* involve in immune regulation; *HOMER1* is associated with neuropsychiatric diseases.
- The association between DEGs (except *CCL22*) and *Toxoplasma* infection is not known.

## CONCLUSION

- Macrophages and dendritic cells are the major cells that transcriptionally respond to *Toxoplasma* infection.
- *Toxoplasma* preferentially targets these phagocytes to replicate and disseminate.
- There is heterogeneity in transcriptional profile during *Toxoplasma*-immune cell interaction via phagocytosis and active invasion.