

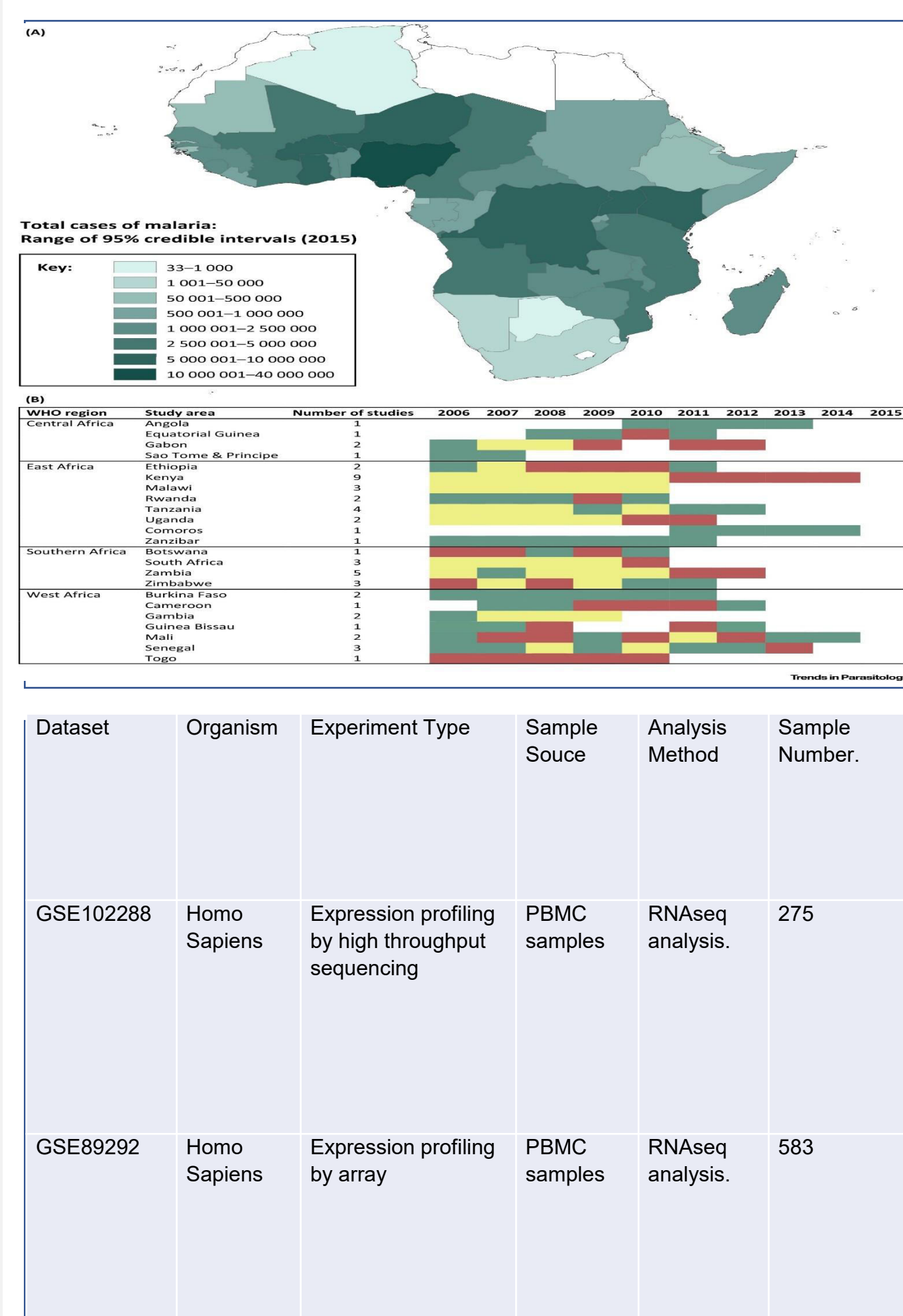
Malaria RTS,S/AS01 Vaccine's Association with Controlled Inflammation and Increased Protection

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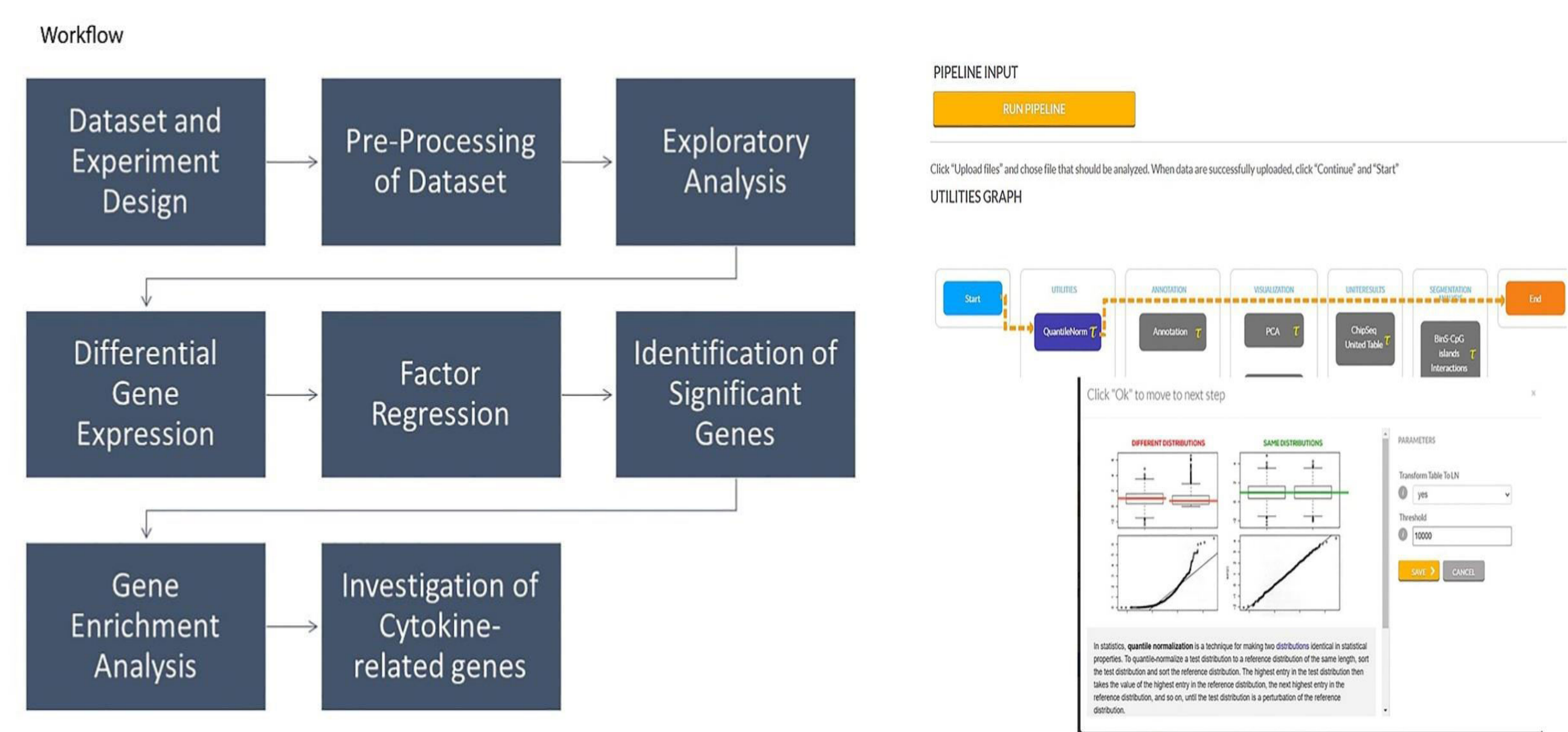
Introduction

In 2019, there were almost 229 million estimated malaria cases worldwide. The number of death from malaria stood near 409,000 in 2019. Africa has faced 94% of all the malaria cases. Although the recent application of RTS,S vaccination has provided a glimpse of hope, further study into variable efficacy of the vaccine is needed to provide better understanding of protective immunity. Thus, the current study is designed to delineate the effect of the different vaccination doses on the transcriptional profiles of subjects to determine its efficacy and understand the molecular mechanisms leading to protection this vaccine provides.



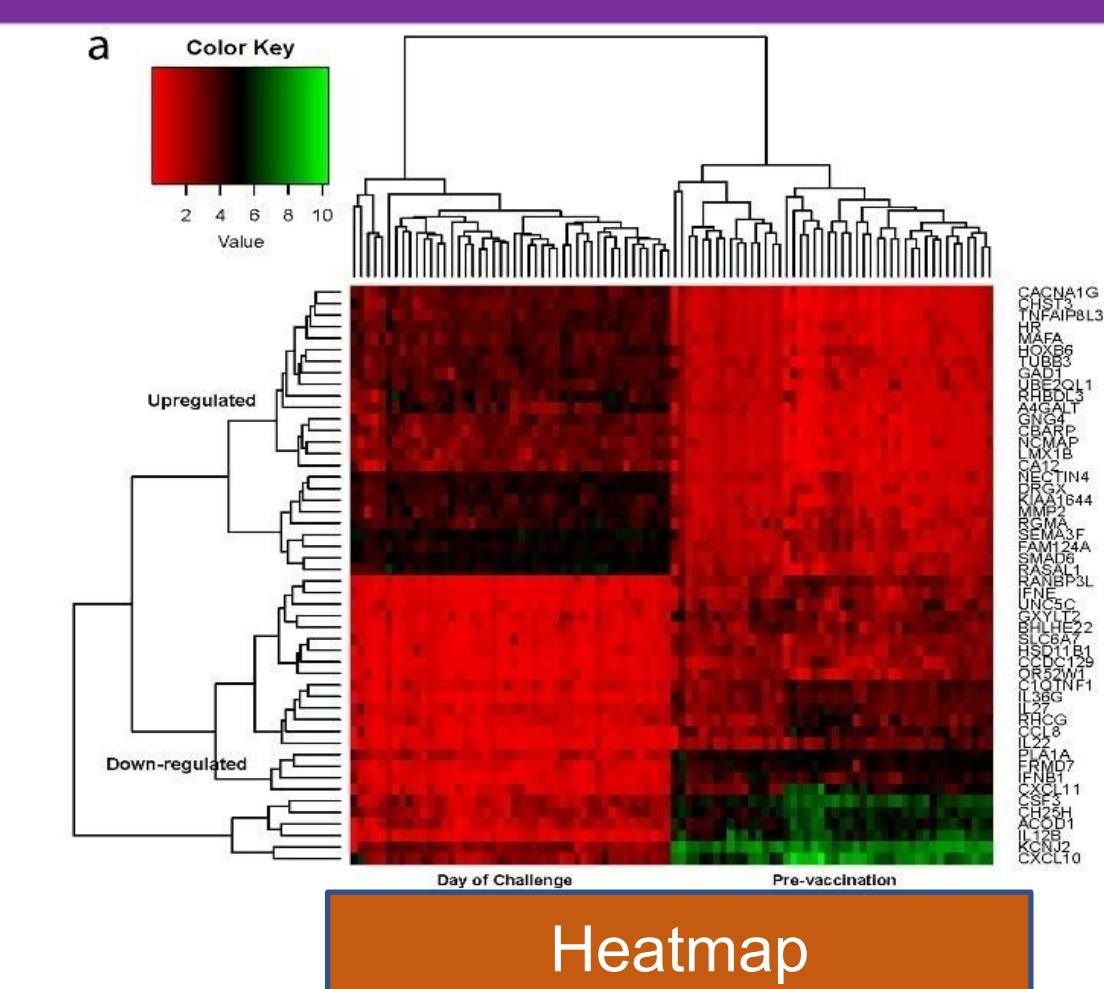
Methods

Two datasets were obtained from GEO with accession numbers GSE102288 and GSE89292. First datasets were normalized. Various Exploratory analysis provided a good outlook on the gene expression of the samples. Differential gene expression analysis was performed by using edgeR. Furthermore, factor regression and gene enrichment analysis was completed with the help of Tbioinfo pipeline and KEGG pathway analysis. Pathway analysis of significantly expressed genes showed association with Cytokine-Chemokine pathway.

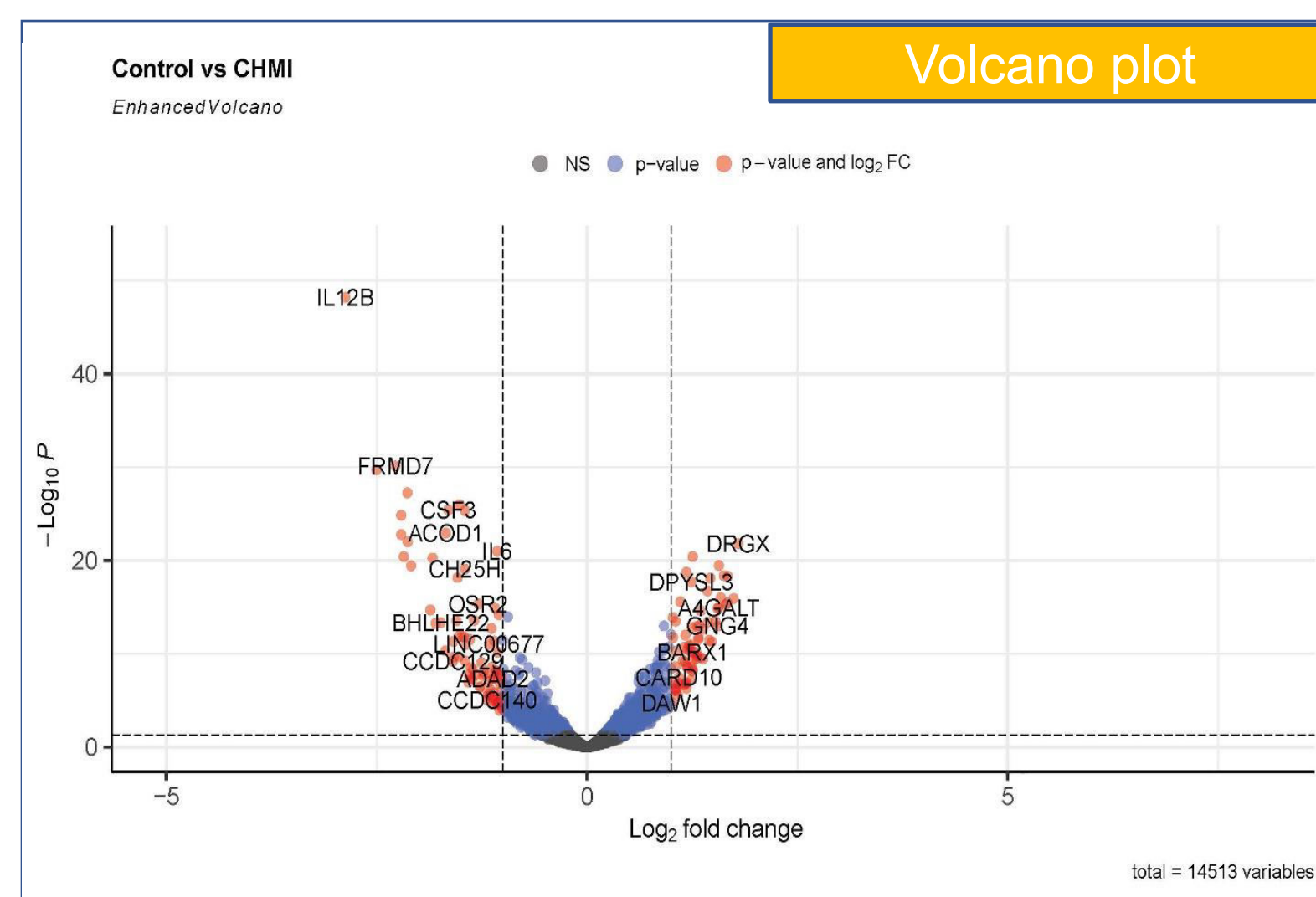


Conclusions

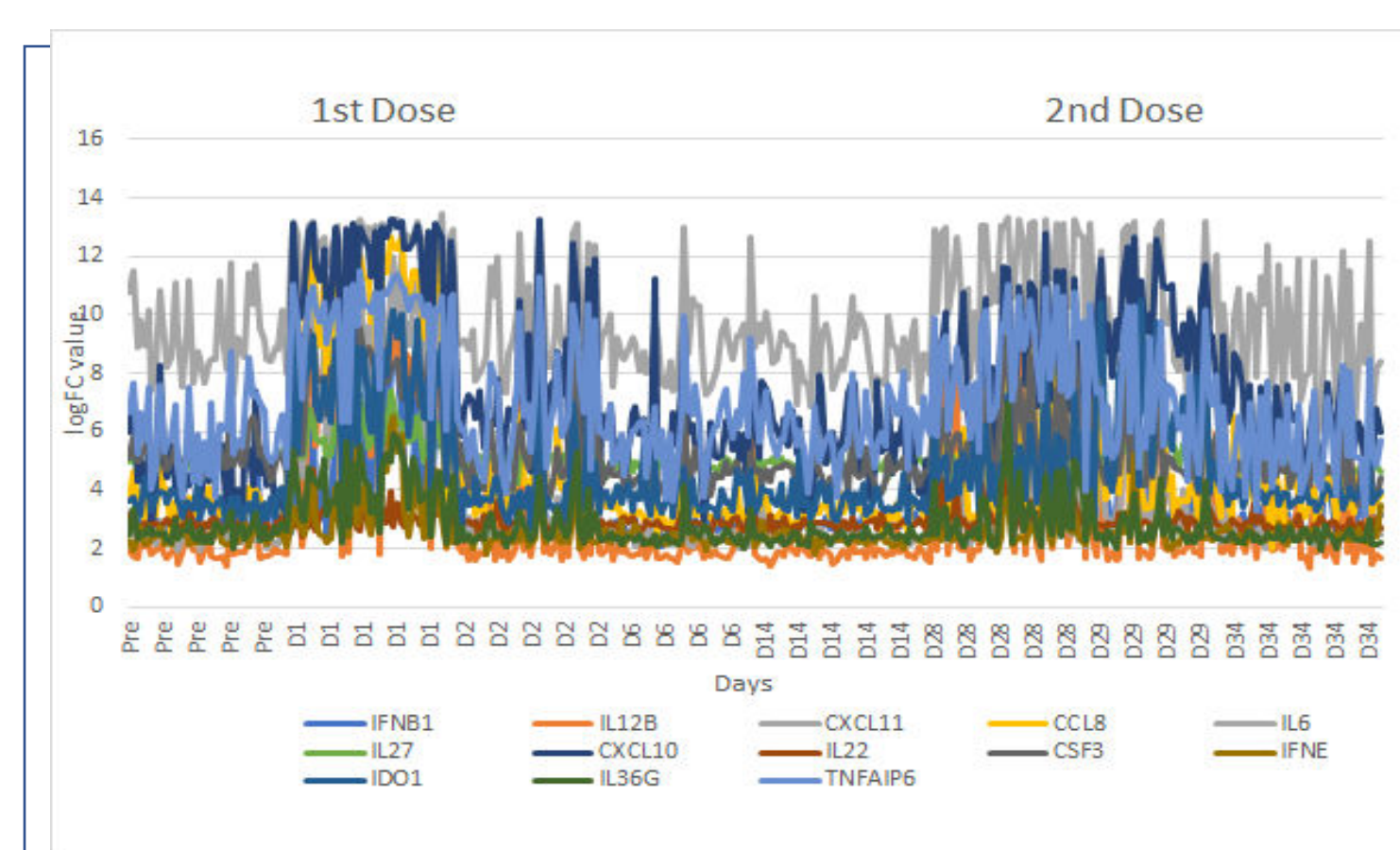
Notably, we identified 13 cytokine genes whose expression significantly varied during three doses. Eventually, these findings give insight to the dual role of cytokine responses in malaria pathogenesis and variations in their expression patterns after various doses of vaccination involved in protection. The downregulation of cytokine and inflammatory genes after 3rd dose was crucial to vaccine protection as it has been found malaria severity and malaria-related death is often associated with inflammatory response. Also, association of significant genes with JAK-STAT and cancer pathways supports previous literatures and suggests further studies.



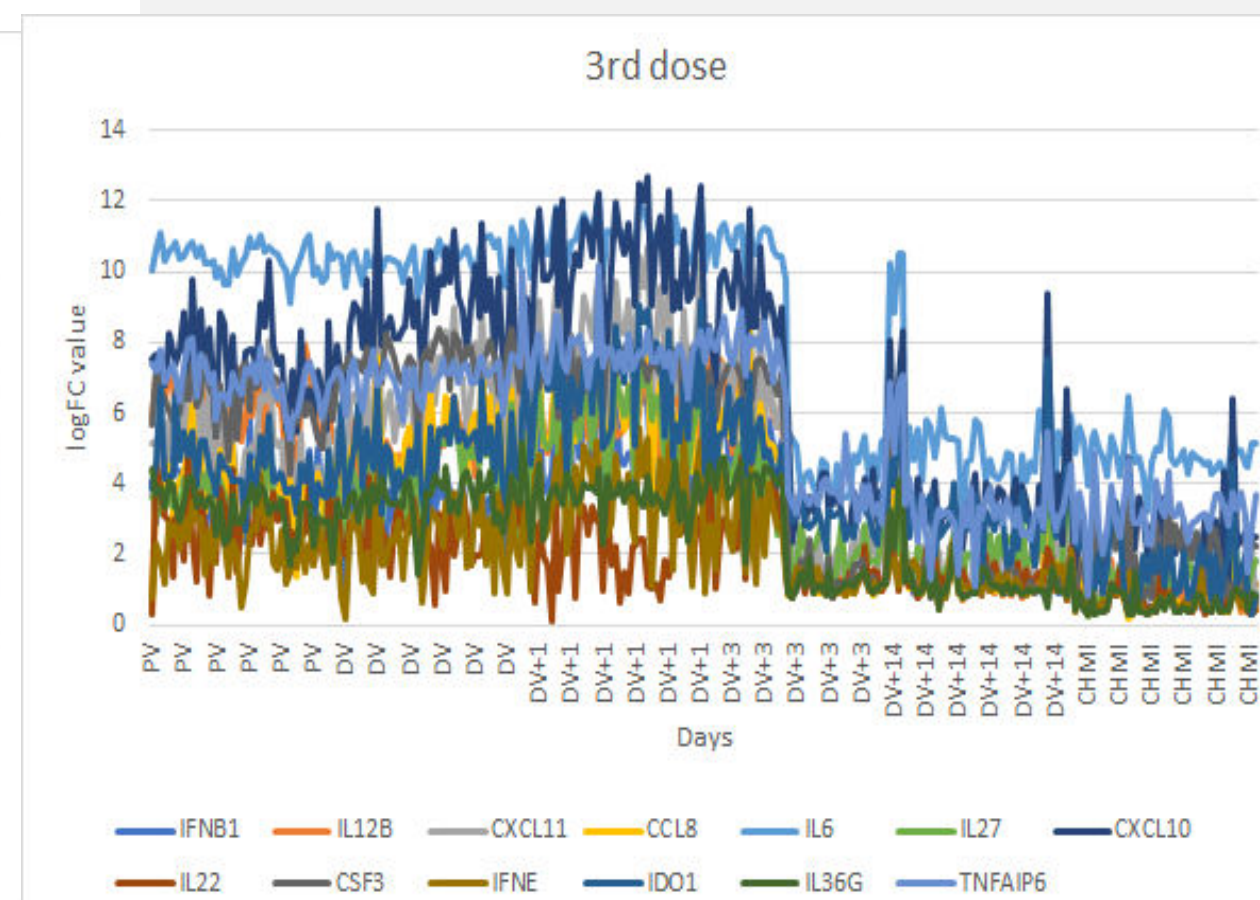
Results



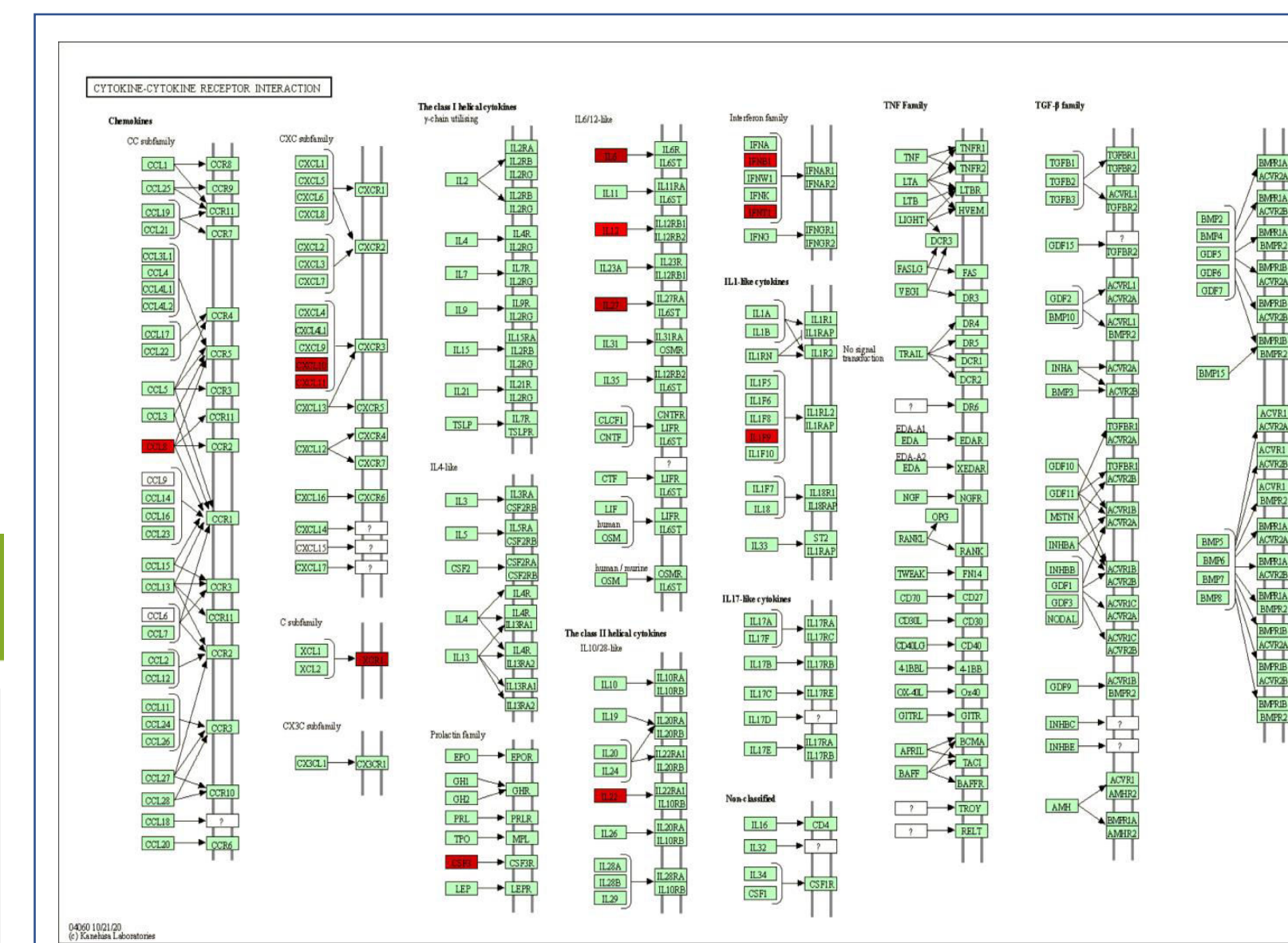
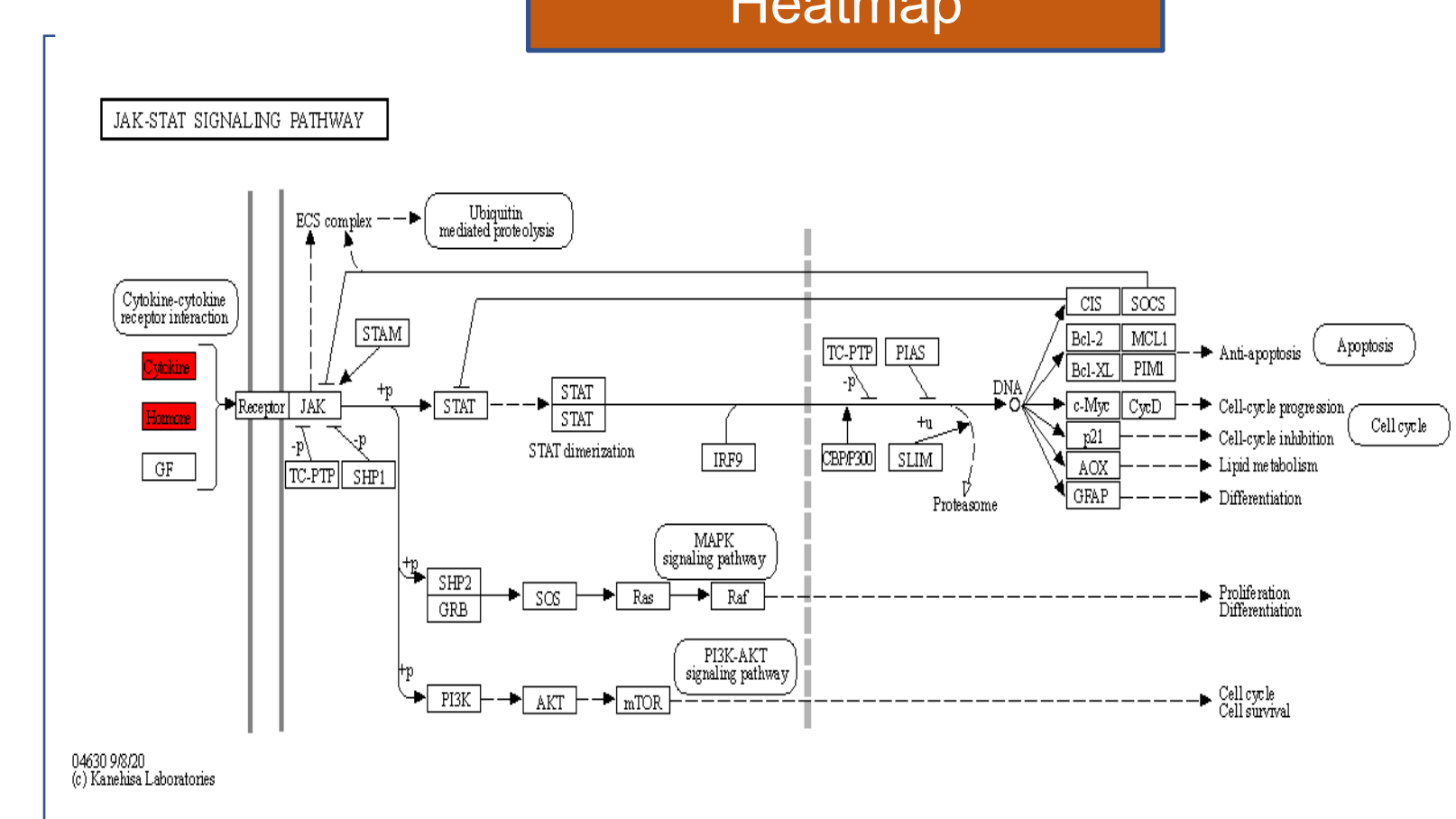
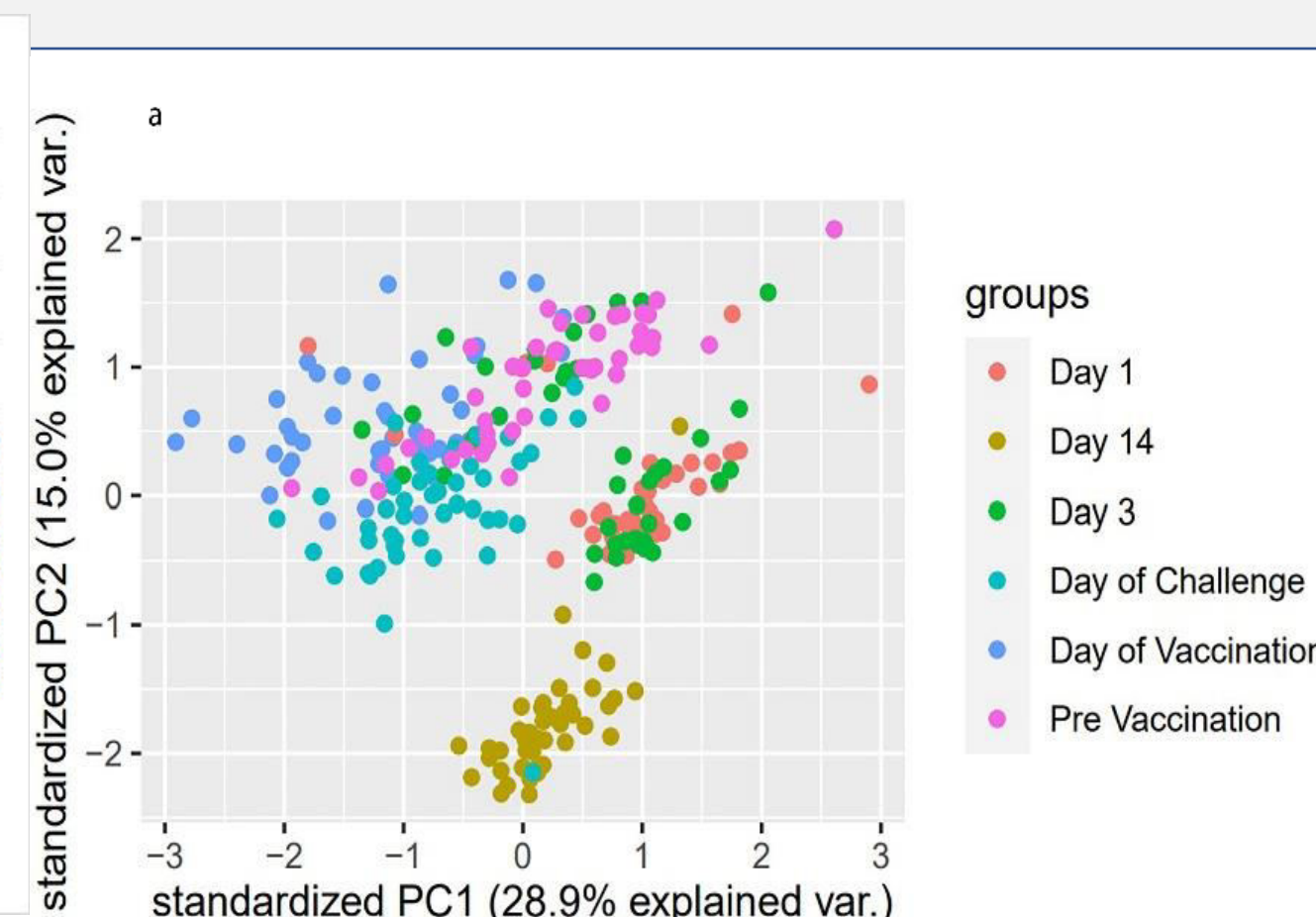
Subsequently, differential gene expression analysis using edgeR revealed the significantly (FDR <0.005) 158 down-regulated and 61 upregulated genes between control vs. Controlled Human Malaria Infection (CHMI) samples. Further, enrichment analysis of significant genes using Annotation and GAGE tools delineate the involvement of *CCL8*, *CXCL10*, *CXCL11*, *XCRI*, *CSF3*, *IFNB1*, *IFNE*, *IL12B*, *IL22*, *IL6*, *IL27*, etc., genes which found to be upregulated after earlier doses but downregulated after the 3rd dose in cytokine-chemokine pathways.



Mostly Upregulation



Downregulation



Pathways in KEGG analysis

Acknowledgements

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