

# Molecular mechanisms underlying cellular aging in controlled human malaria infection (CHMI)

Shirin Akhter<sup>1,2#</sup>, Amani Odeh<sup>1,2#</sup>, Aurelie Miglar<sup>1,2</sup>, Pengjun Xi<sup>1,2</sup>, Isaie J. Reuling<sup>3</sup>, Xi Zen Yap<sup>3</sup>, Robert W. Sauerwein<sup>3</sup>, Muhammad Asghar<sup>1,2\*</sup>

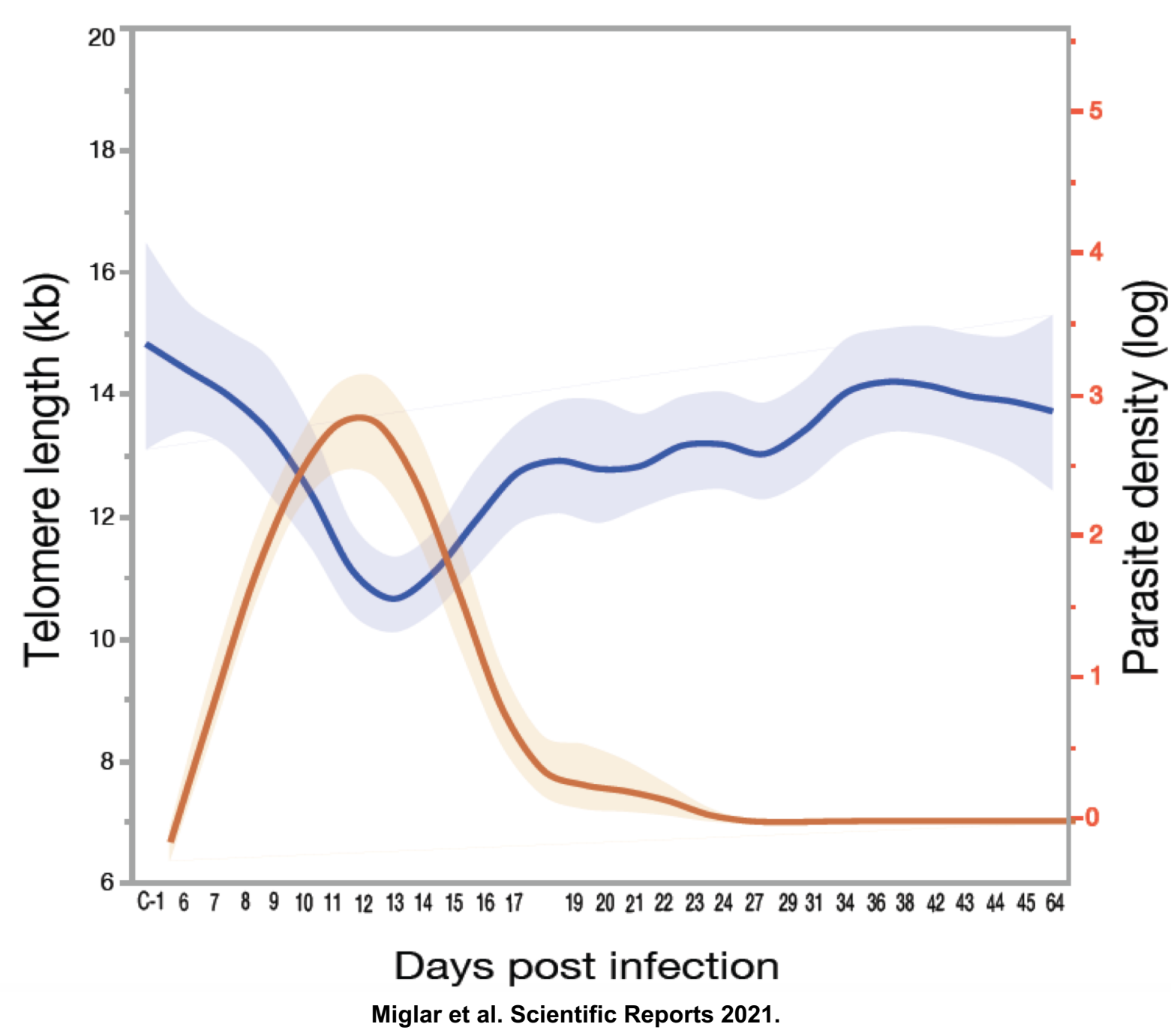
<sup>1</sup>Division of Infectious Diseases, Department of Medicine Solna, Karolinska Institutet, Sweden.

<sup>2</sup>Department of Infectious Diseases, Karolinska University Hospital, Sweden.

<sup>3</sup>Department of Medical Microbiology, Radboud University Medical Center, Geert Grooteplein 28, Microbiology 268, 6500 HB, Nijmegen, The Netherlands.

## Introduction:

- Acute Malaria infection has a pronounced effect on cellular aging.
- The clinical consequences of acute malaria are well known, but the host could have a hidden long-term cost.
- A previous study showed that malaria infection (CHMI) accelerated telomere shortening (Miglar et al. Sci report 201).

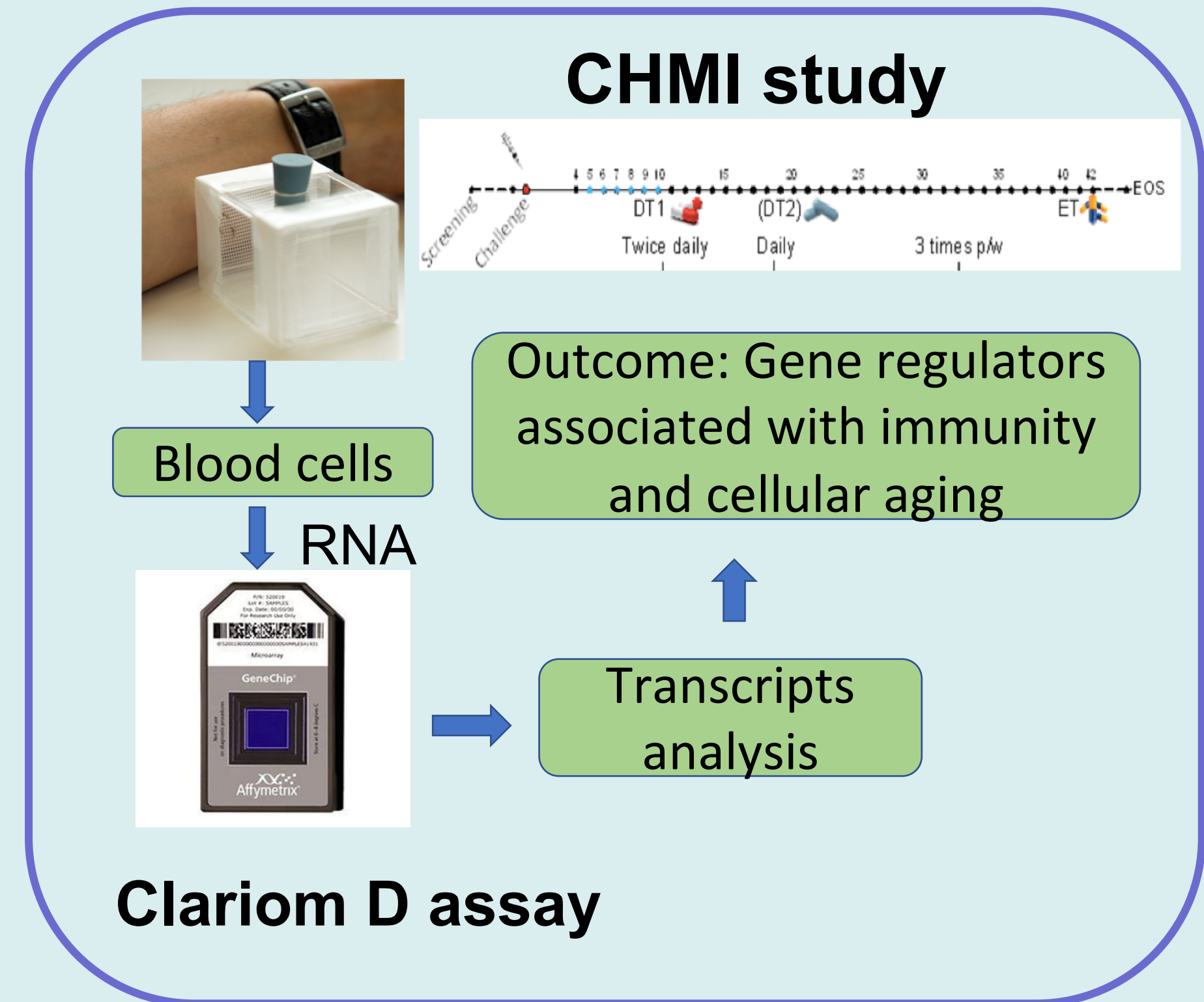


Miglar et al. Scientific Reports 2021.

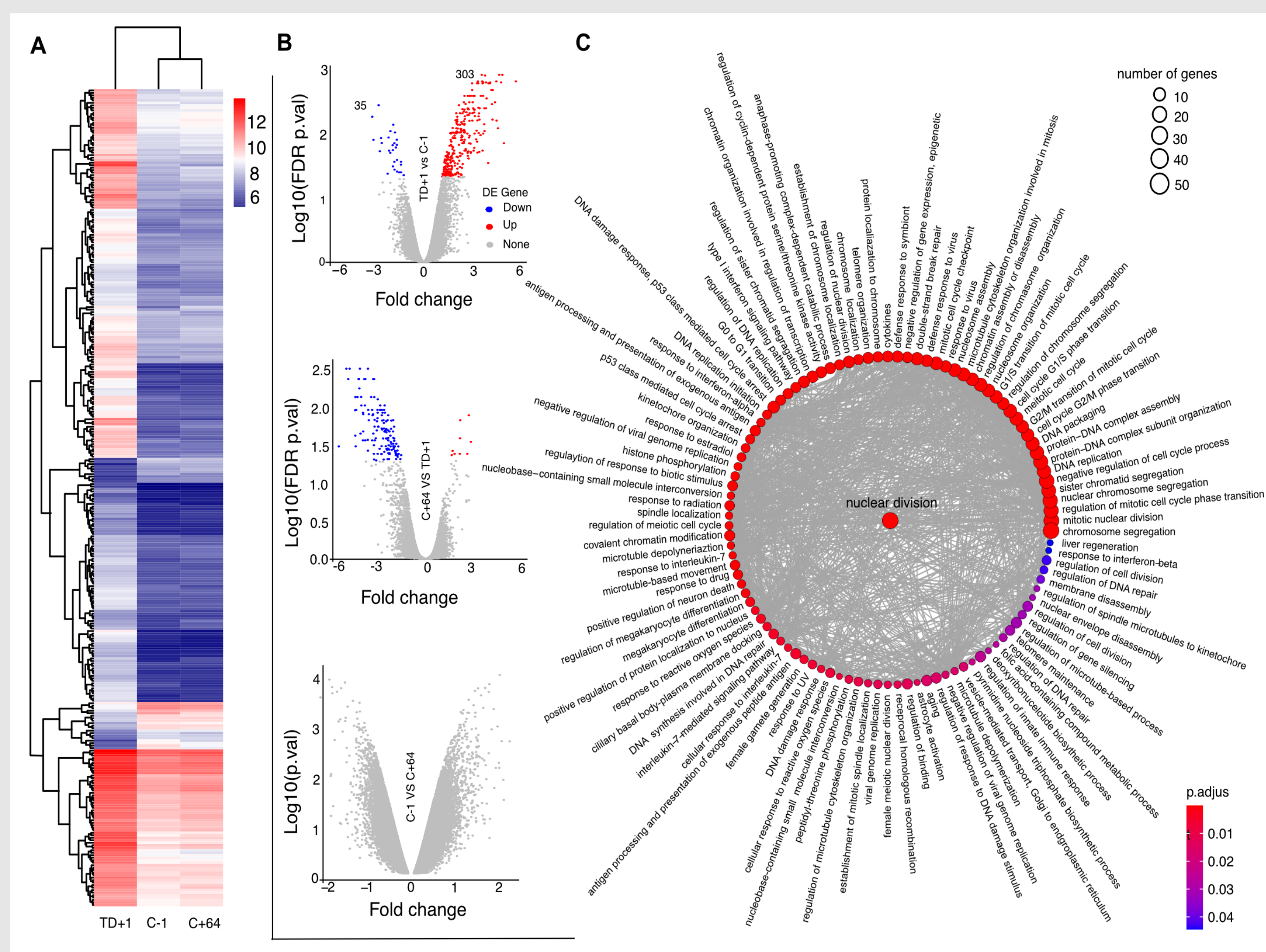
**Conclusions:** Transcriptome studies in CHMI showed important gene regulators associated with immunity and cellular aging during infection. But, the effect was fully reversed after successful treatment.

**Aim:** To study transcriptional regulation underlying cellular aging in controlled human malaria infection.

## Method:

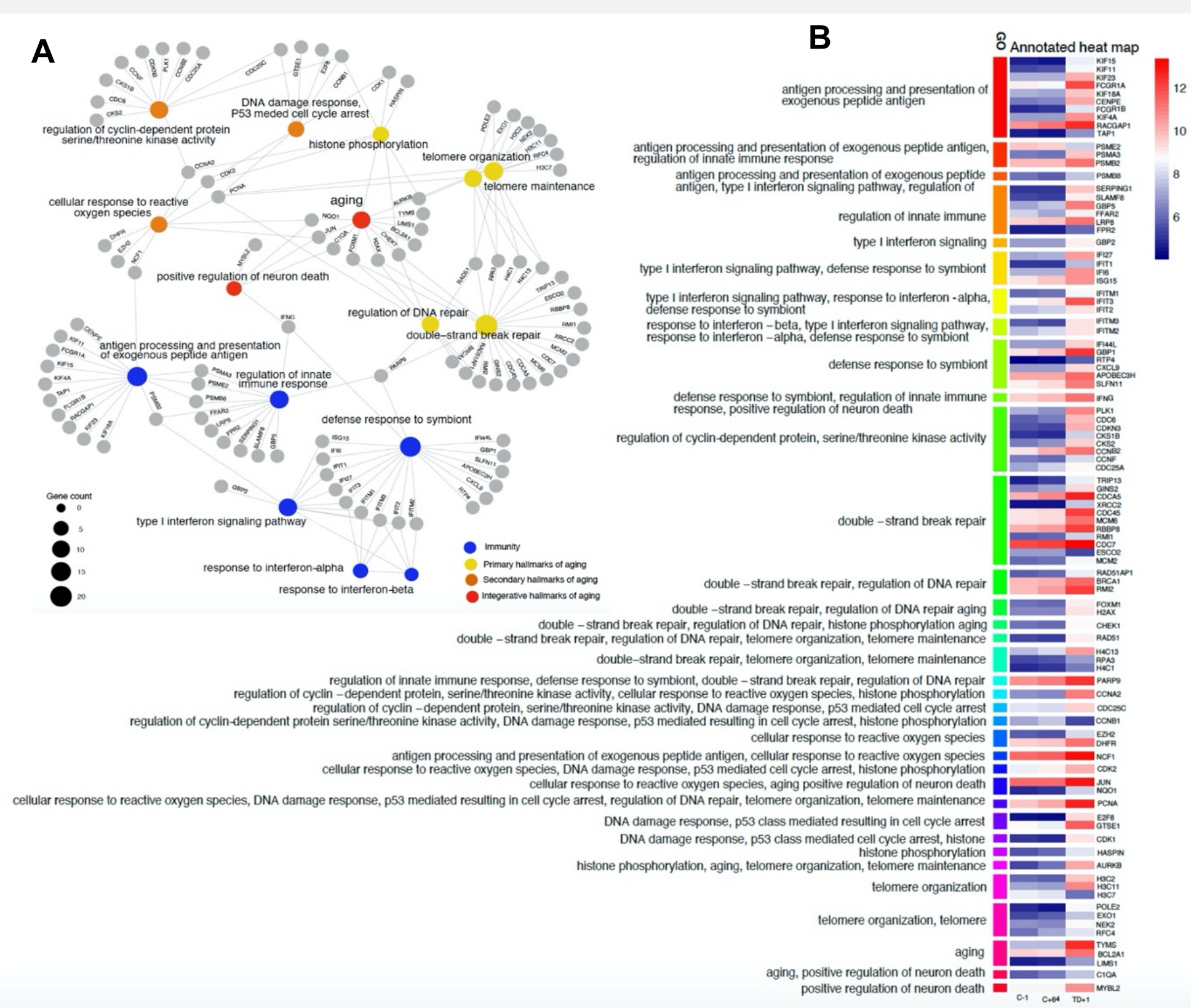


Transcriptome analysis showed distinct gene expression during infection in controlled Malaria infection (see: figure 1 A & B).



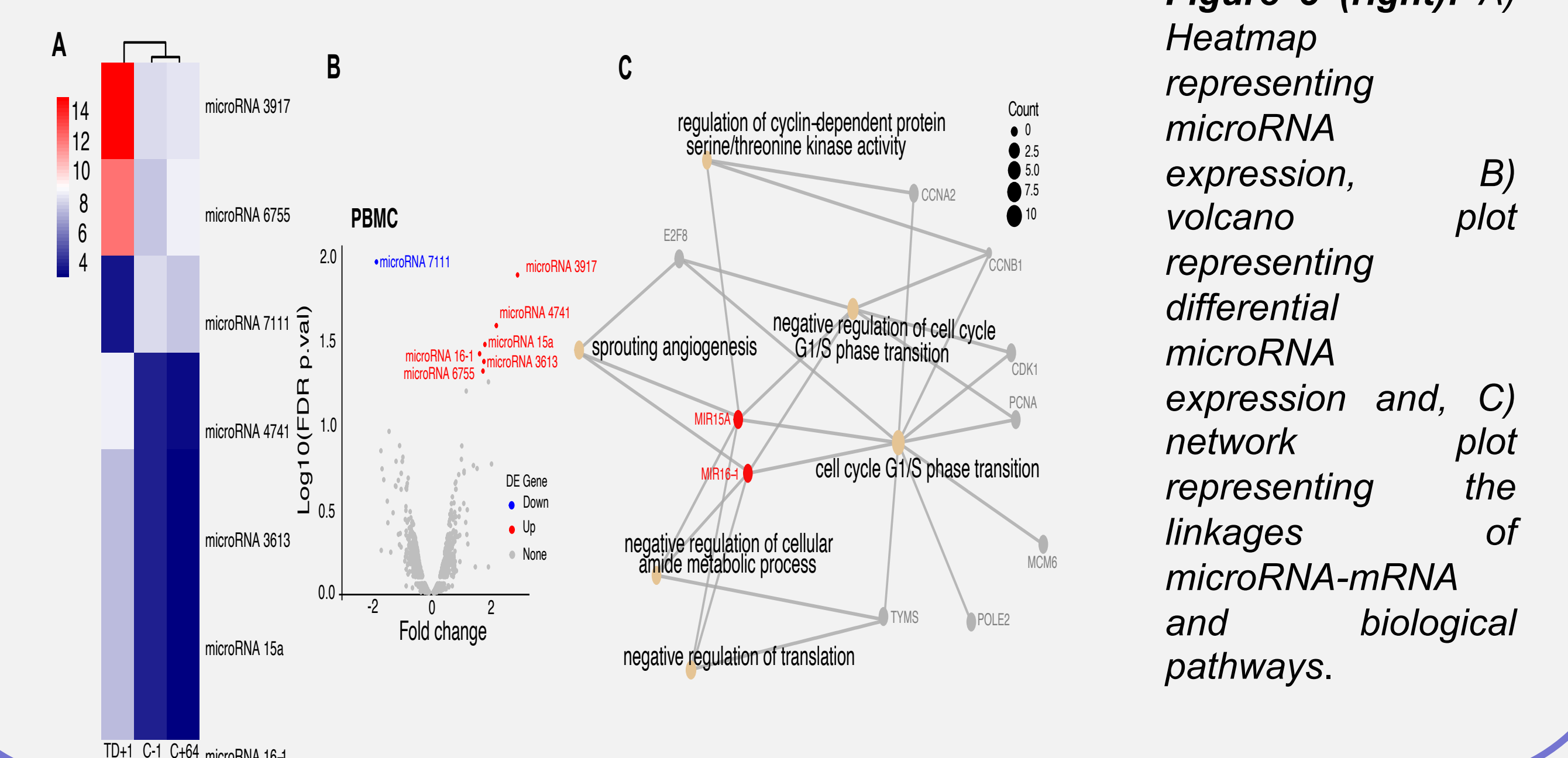
**Figure 1:** A) Heatmap of differentially expressed genes. The column TD+1 represents the infected time point, C-1 represents non-infected control, and C+64 represents the recovery time point. B) Volcano plots of differentially expressed genes in paired comparisons; TD+1 vs C-1 (during infection vs control), C64 vs TD+1 (recovery vs during infection), and C-1 vs C+64 (control vs recovery). C) Gene Ontology enrichment of differentially expressed genes.

Functionally enriched genes are associated with immunity and different categories hallmarks of aging in controlled malaria infection (see: figure 2 A).



**Figure 2 (left):** A) Network plot representing linkages of important gene regulators and biological pathways; B) Annotated Heatmap representing biological pathways together with gene expressions at C-1 (control), recovery (C+64), and TD+1 (during infection). Annotation at left represents biological pathways, and annotation at right shows gene names.

Co-expression of microRNA and mRNA showed a possible involvement in cell cycle arrest in controlled malaria infection (see: figure 3 A,B&C).



**Figure 3 (right):** A) Heatmap representing microRNA expression, B) volcano plot representing differential microRNA expression and, C) network plot representing the linkages of microRNA-mRNA and biological pathways.

Karolinska Institutet

Shirin Akhter

Title: Postdoctoral researcher

Visiting address: Bioclinicum J7:20, Akademiska Stråket 1, 17164 Solna.

Postal address: K2 medicin Solana,

K2 infection M Asghar, 17177, Stockholm

Email: [shirin.akhter@ki.se](mailto:shirin.akhter@ki.se), [shirin.akhter.biotech@gmail.com](mailto:shirin.akhter.biotech@gmail.com)



Karolinska Institutet