

Experimental reverse zoonosis of *Plasmodium falciparum* in mouse erythrocytes reveals key cellular pathways for anti-malarial drug discovery

Erica Lee Qian Hui^{1,2}, Jaishree Tripathi^{1,4}, Samaksh Singh¹, Shifana Raja Abdeen³, Jing Wen Hang^{1,2}, Zbynek Bozdech⁴, Kevin S. W. Tan^{1,5}, Benoit Malleret^{1,2,3}

¹Department of Microbiology and Immunology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

²Immunology Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³Singapore Immunology Network, Agency for Science, Technology and Research, Singapore

⁴School of Biological Sciences, Nanyang Technological University, Singapore

⁵Healthy Longevity Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

INTRODUCTION

Malaria

In 2022,
249 million cases¹
608,000 deaths¹

Dormancy

- Temporary growth arrest
- Presence of pyknotic rings
- Hypothermic and hyperthermic conditions can result in dormancy²

P. falciparum erythrocyte invasion

- Host receptor-parasite ligand interactions
- PfRH5 binds to erythrocyte receptor CD147³

P. falciparum animal models

Non-human primates

Humanized mice
(Liver-humanized/hRBC
engraftment)

Ethical and cost issues⁴

Hostile mouse environment
and need for
immunocompromised mice⁵

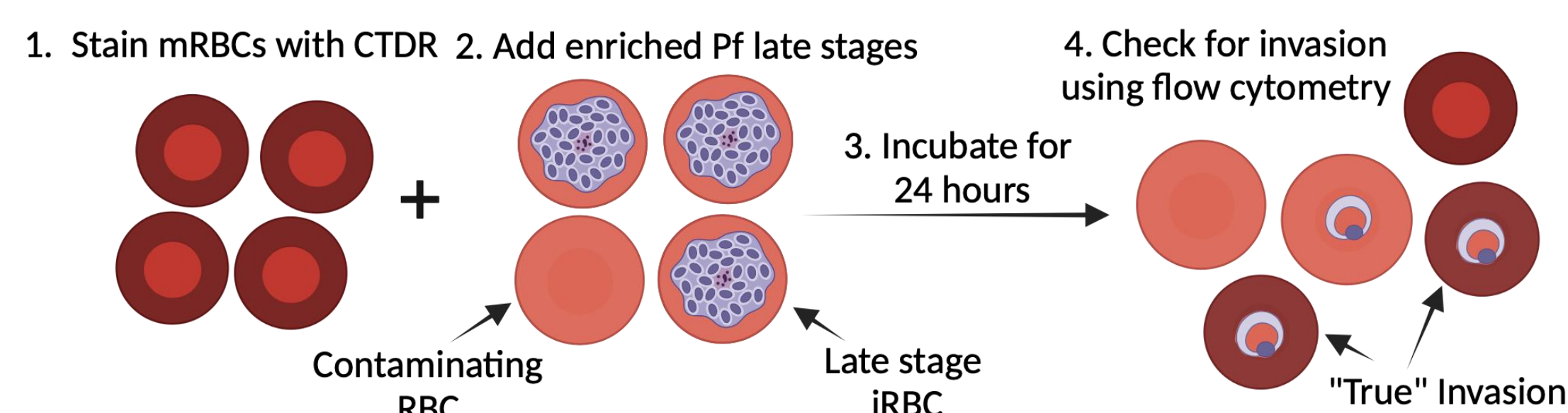
Research gap

Essential parasite pathways to circumvent drug resistance

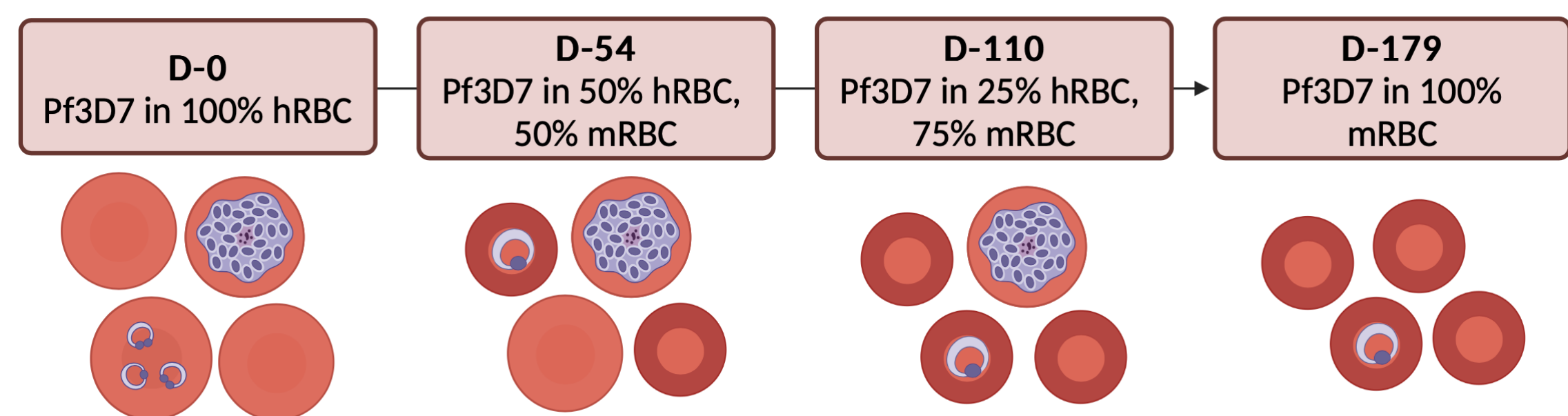
PROJECT AIMS & METHODS

Aim 1: To culture and adapt *P. falciparum* in mouse RBCs *in vitro*

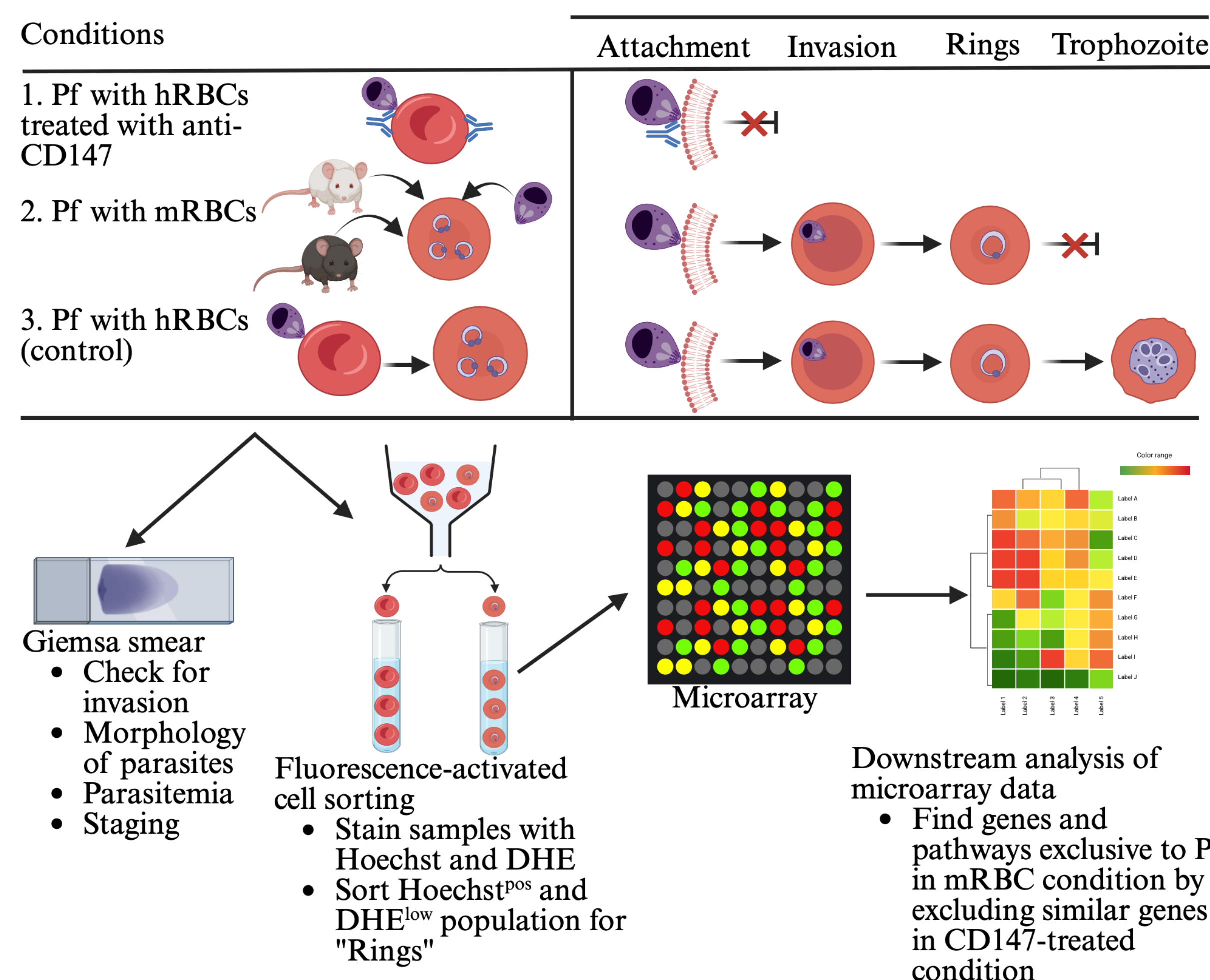
- Pf3D7 in mRBC Invasion Assay⁶



- Pf3D7 in mRBC Long-term Adaptation⁷



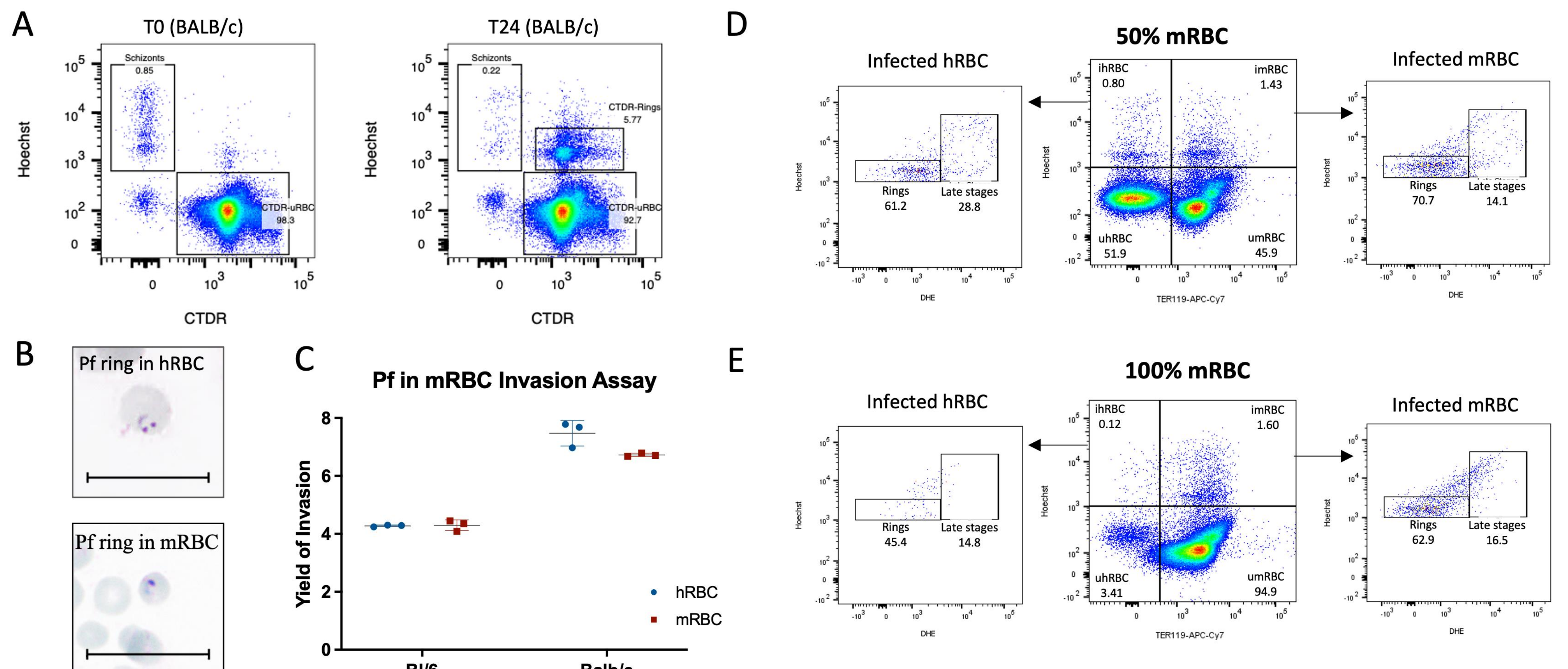
Aim 2: To study the transcriptomics of *P. falciparum* in mouse RBCs



RESULTS AND DISCUSSION

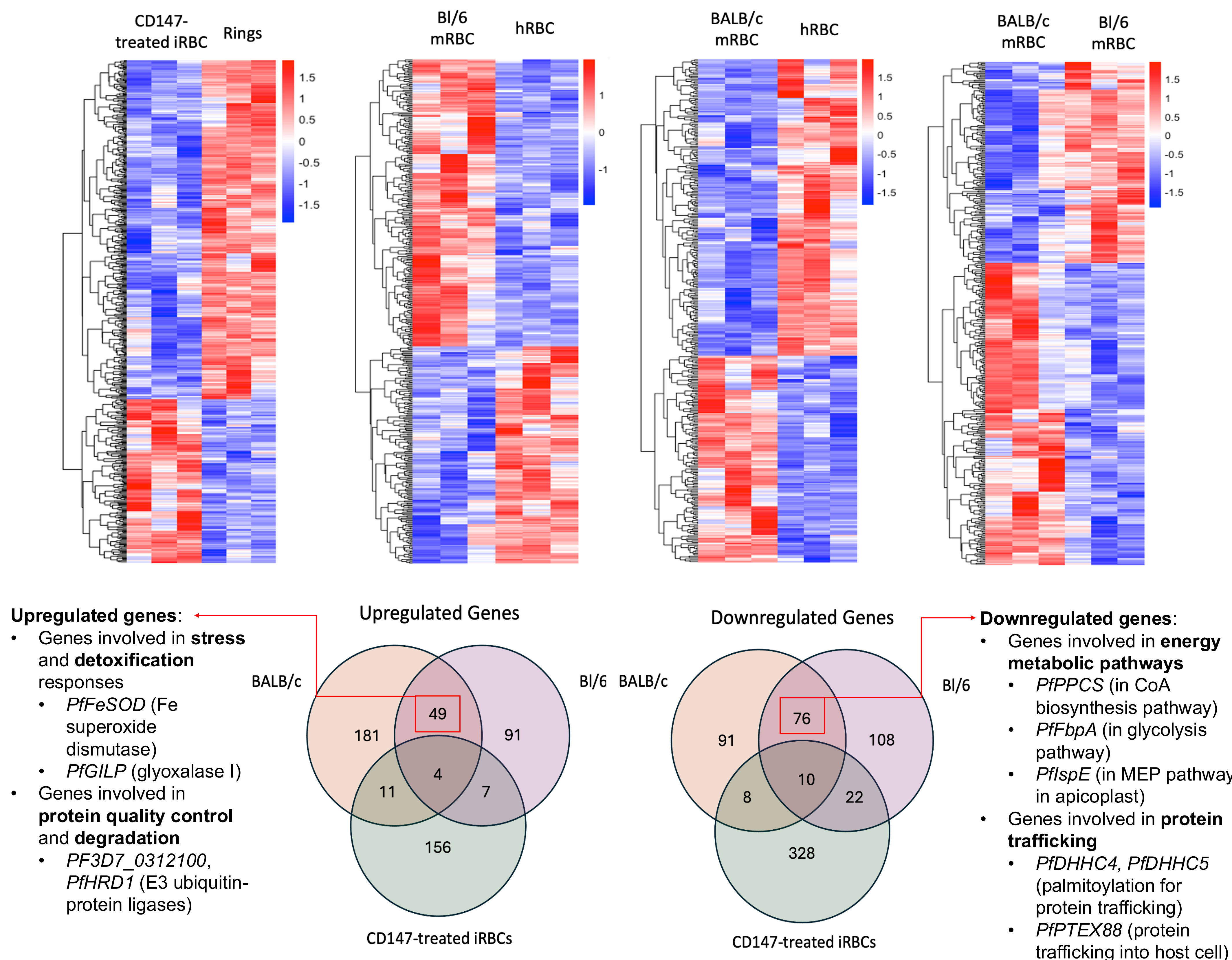
AIM 1: TO CULTURE AND ADAPT *P. FALCIPARUM* IN MOUSE RBCS *IN VITRO*

1.1 *P. falciparum* can invade but is unable to adapt into mouse RBCs after 6 months



AIM 2: TO STUDY THE TRANSCRIPTOMICS OF *P. FALCIPARUM* IN MOUSE RBCS

2.1 DEG analysis



CONCLUSIONS

AIM 1:

- Pf3D7 can invade mRBCs and develop into rings
- Pf3D7 is unable to adapt into mouse RBCs after 6 months

AIM 2:

- Upregulated genes suggest elevated oxidative or metabolic stress and proteostasis → parasite adaption to a different intracellular environment
- Downregulated genes suggest reduced or altered energy metabolism and protein trafficking → transcriptionally inactive state

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