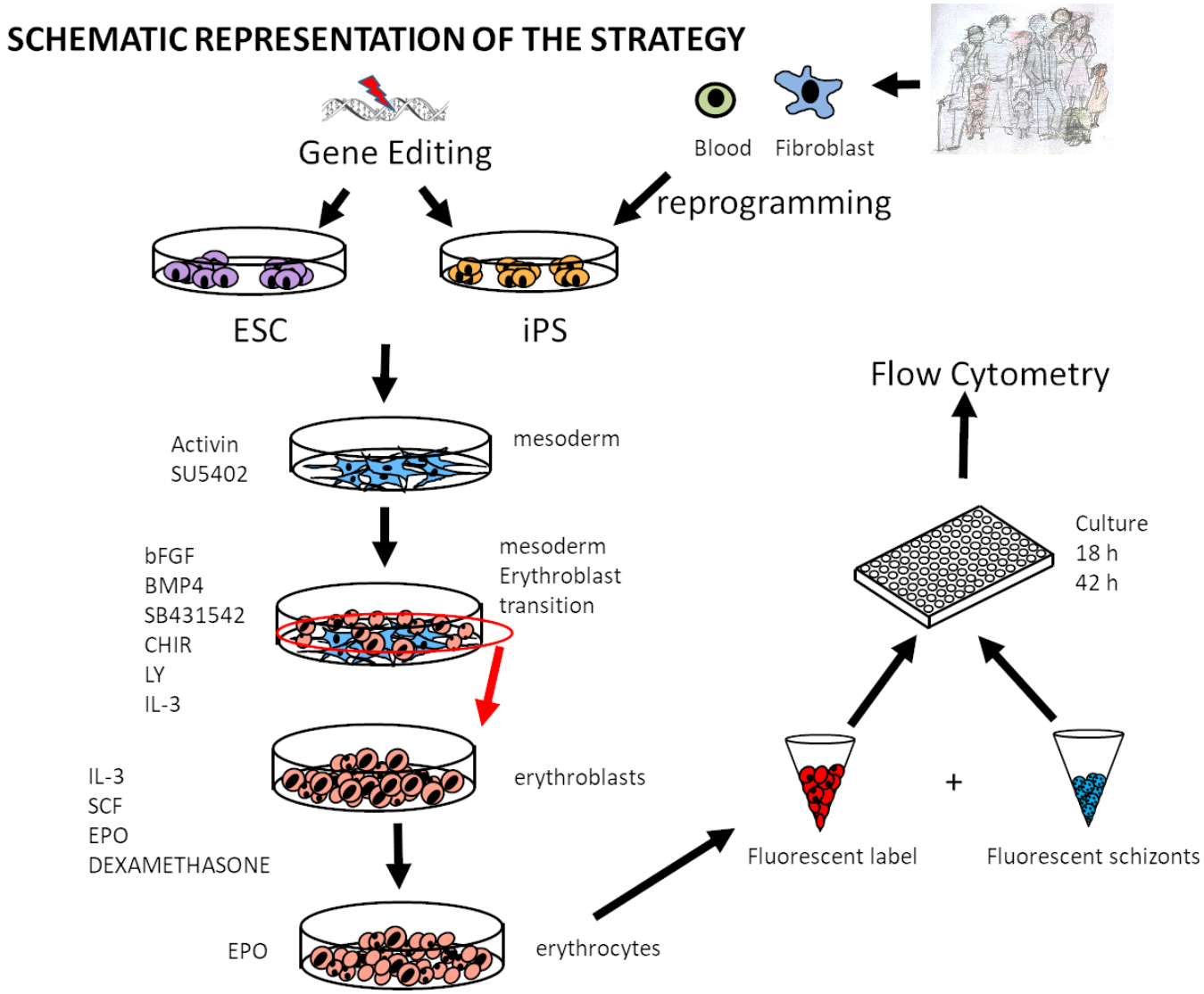
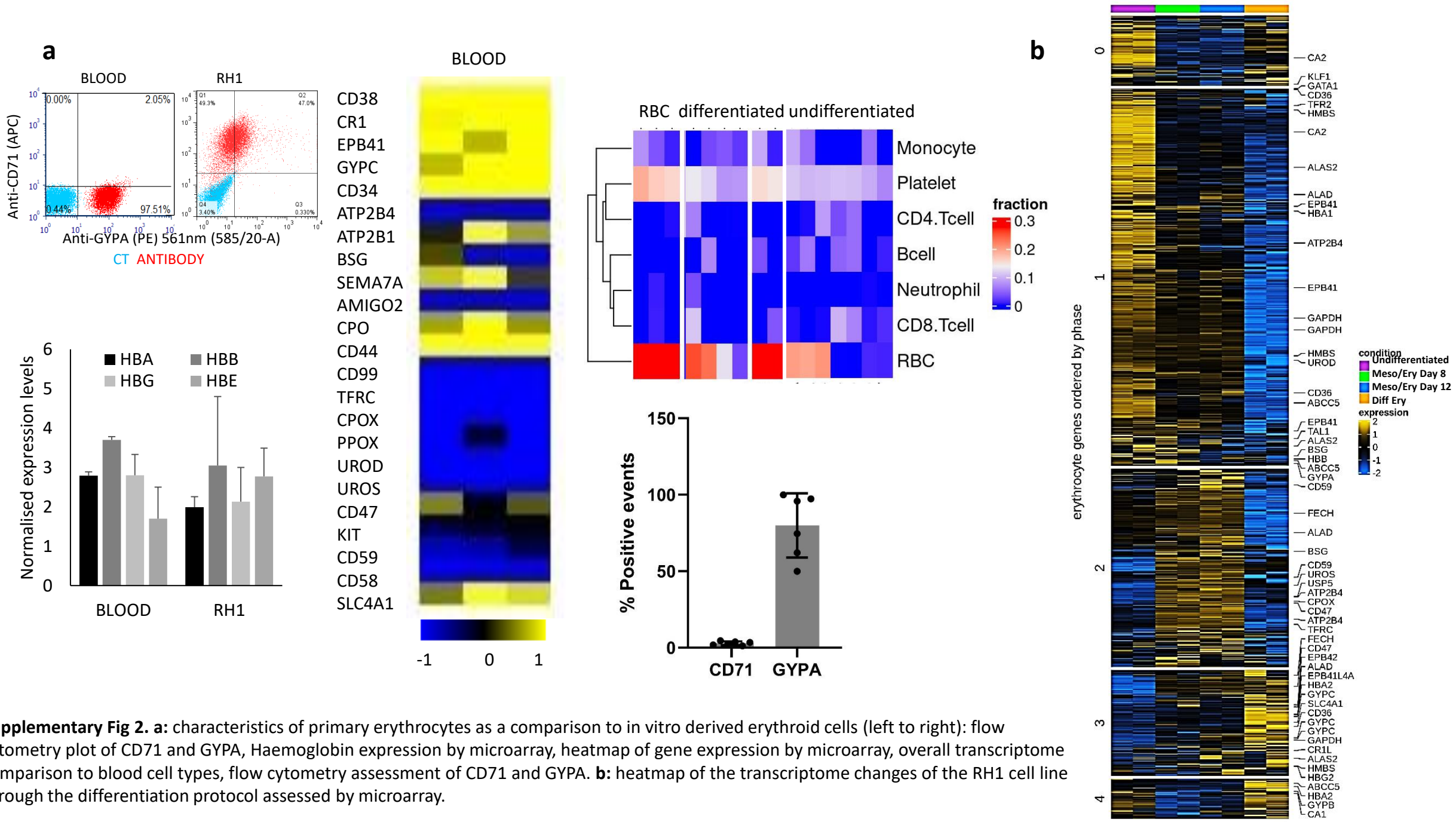
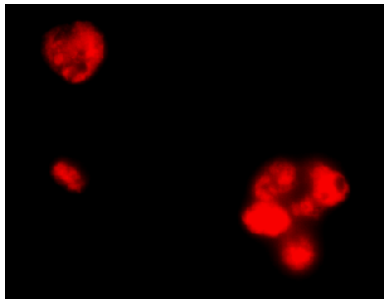


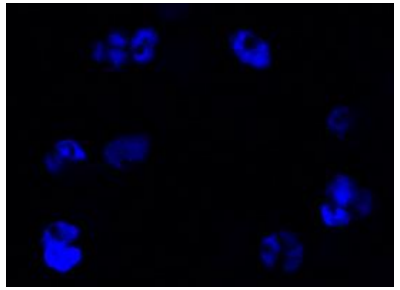
Supplementary Fig 1: schematic representation of the strategy to generate erythroid cells *in vitro* pluripotent stem cells of diverse origin to assess invasion by *P. falciparum*



Supplementary Fig 2. a: characteristics of primary erythrocytes as a comparison to in vitro derived erythroid cells (left to right): flow cytometry plot of CD71 and GYPA, Haemoglobin expression by microarray, heatmap of gene expression by microarray, overall transcriptome comparison to blood cell types, flow cytometry assessment of CD71 and GYPA. **b:** heatmap of the transcriptome changes of the RH1 cell line through the differentiation protocol assessed by microarray.



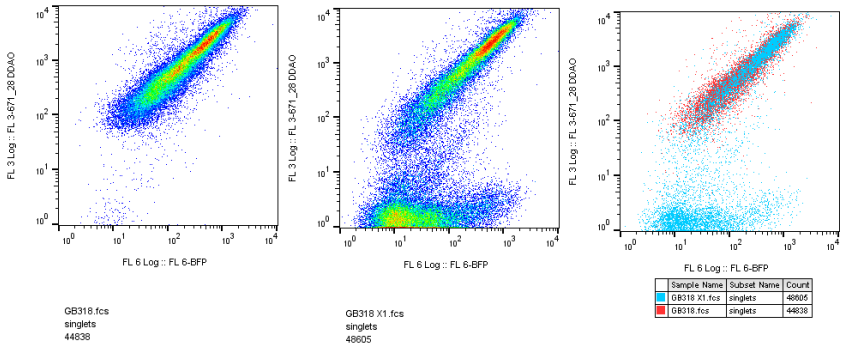
PURIFY SCHIZONTS

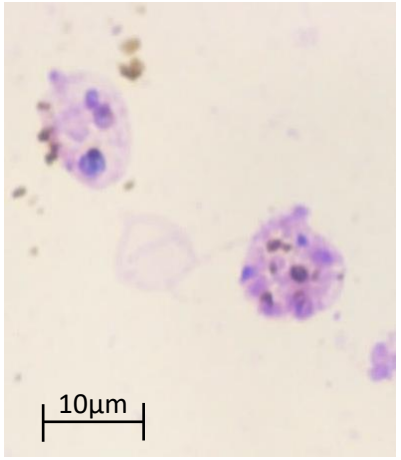


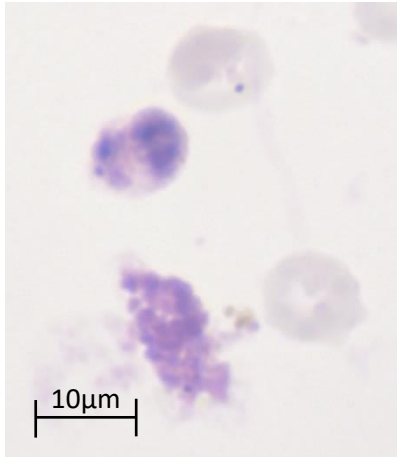
DDAO LABELLED DIFFERENTIATED IPS CELLS + FLUORESCENT (BFP) PARASITES

CULTURE IN 96 WELL PLATES FOR 18 H & 42 H

FLOW CYTOMETRY

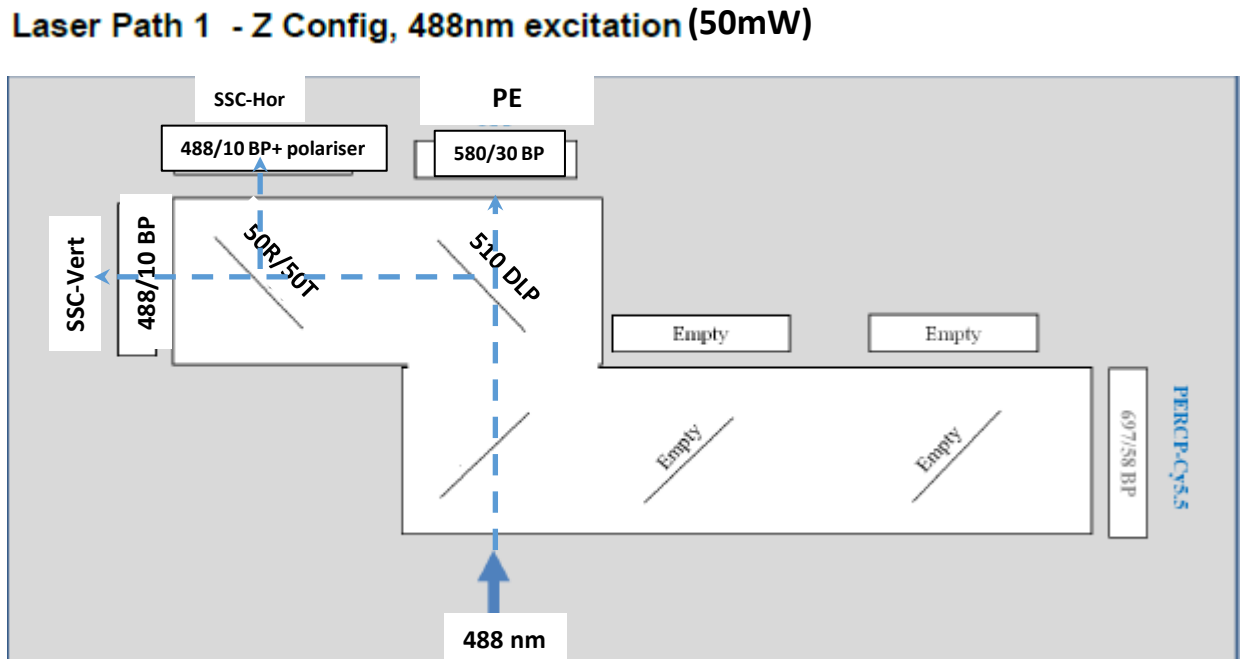




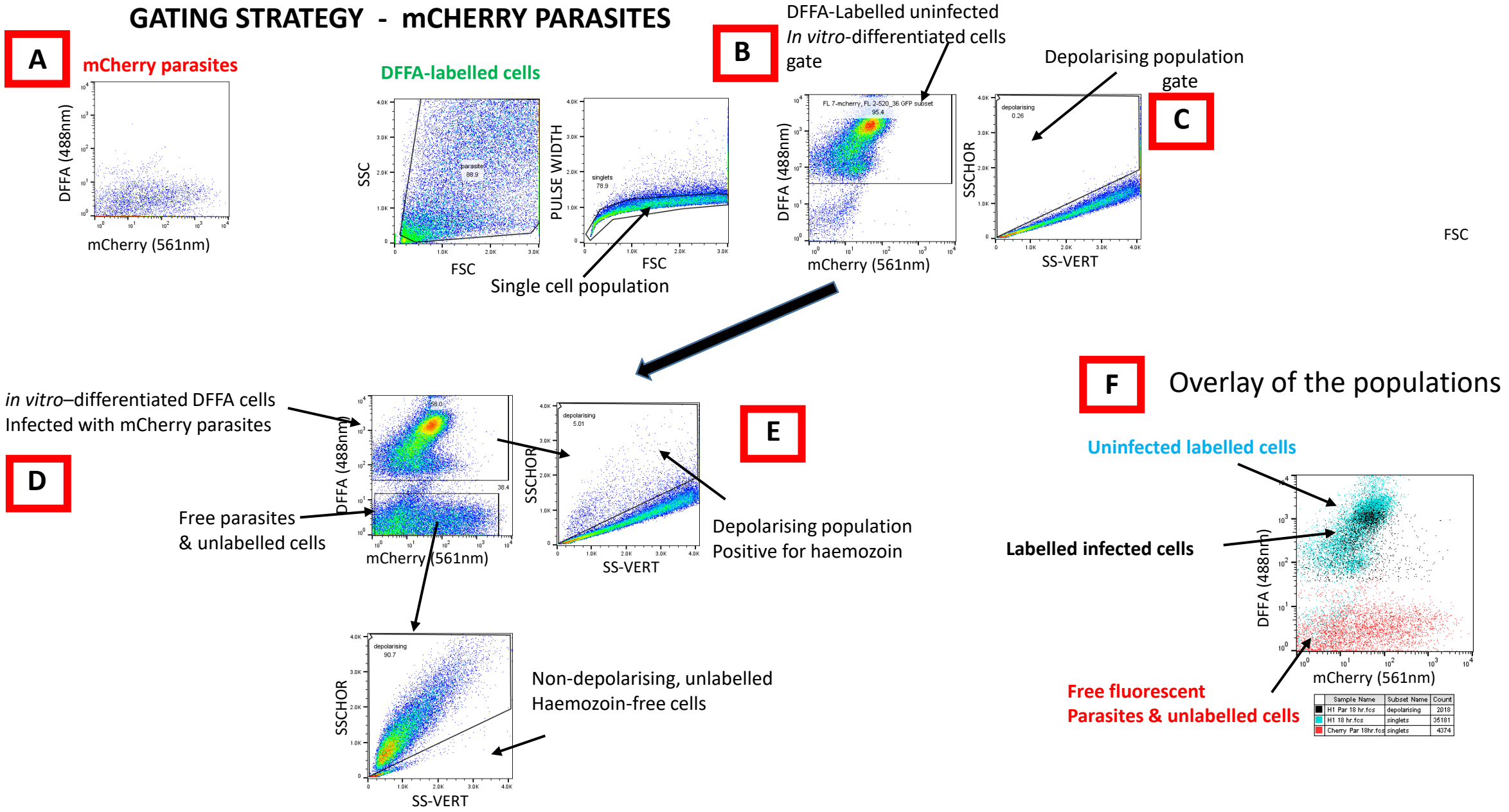


Supplementary Fig 3: design of the invasion assay developed to assess infectivity of *P. falciparum* into *in vitro* derived erythroid cells

MO-FLO FLOW CYTOMETRY OPTICS LAYOUT

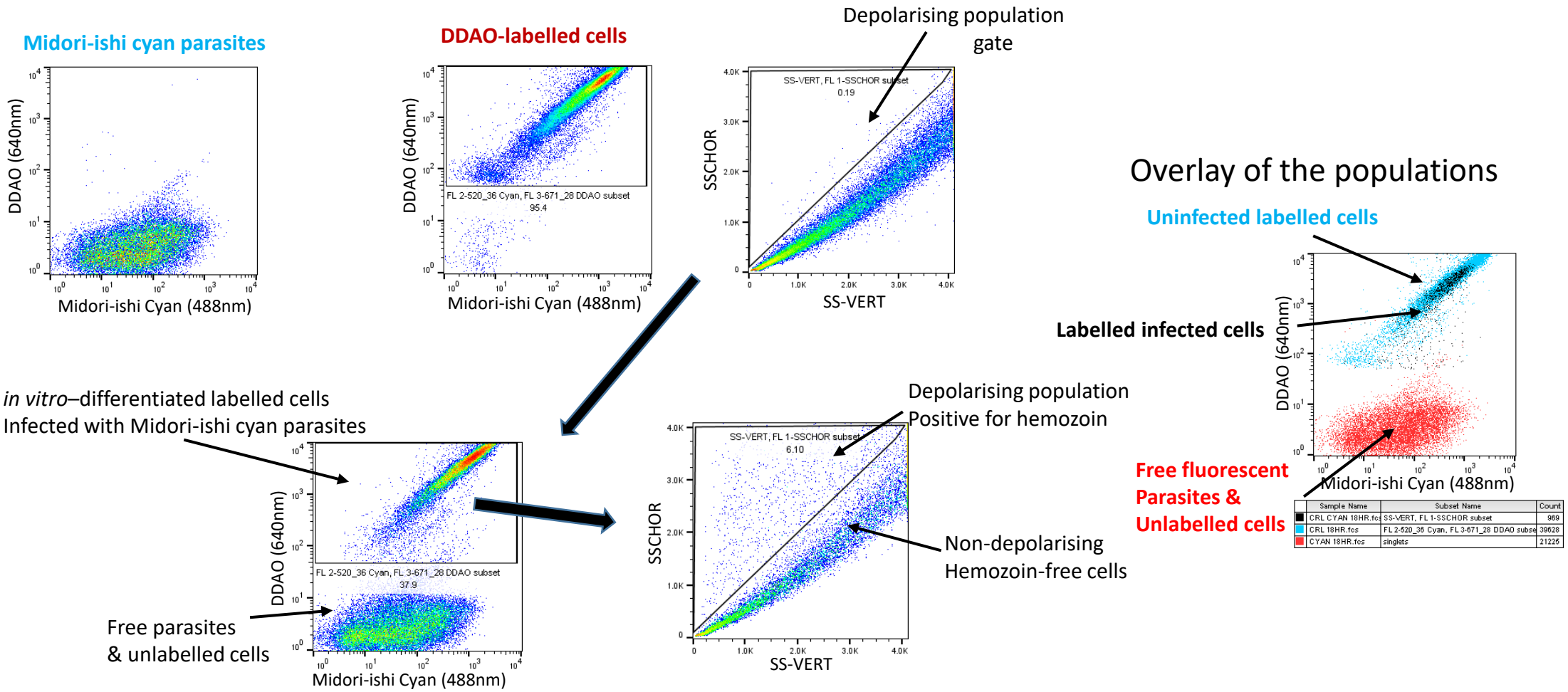


Supplementary Fig 4: set up of the flow cytometer to detect hemozoin by light depolarisation



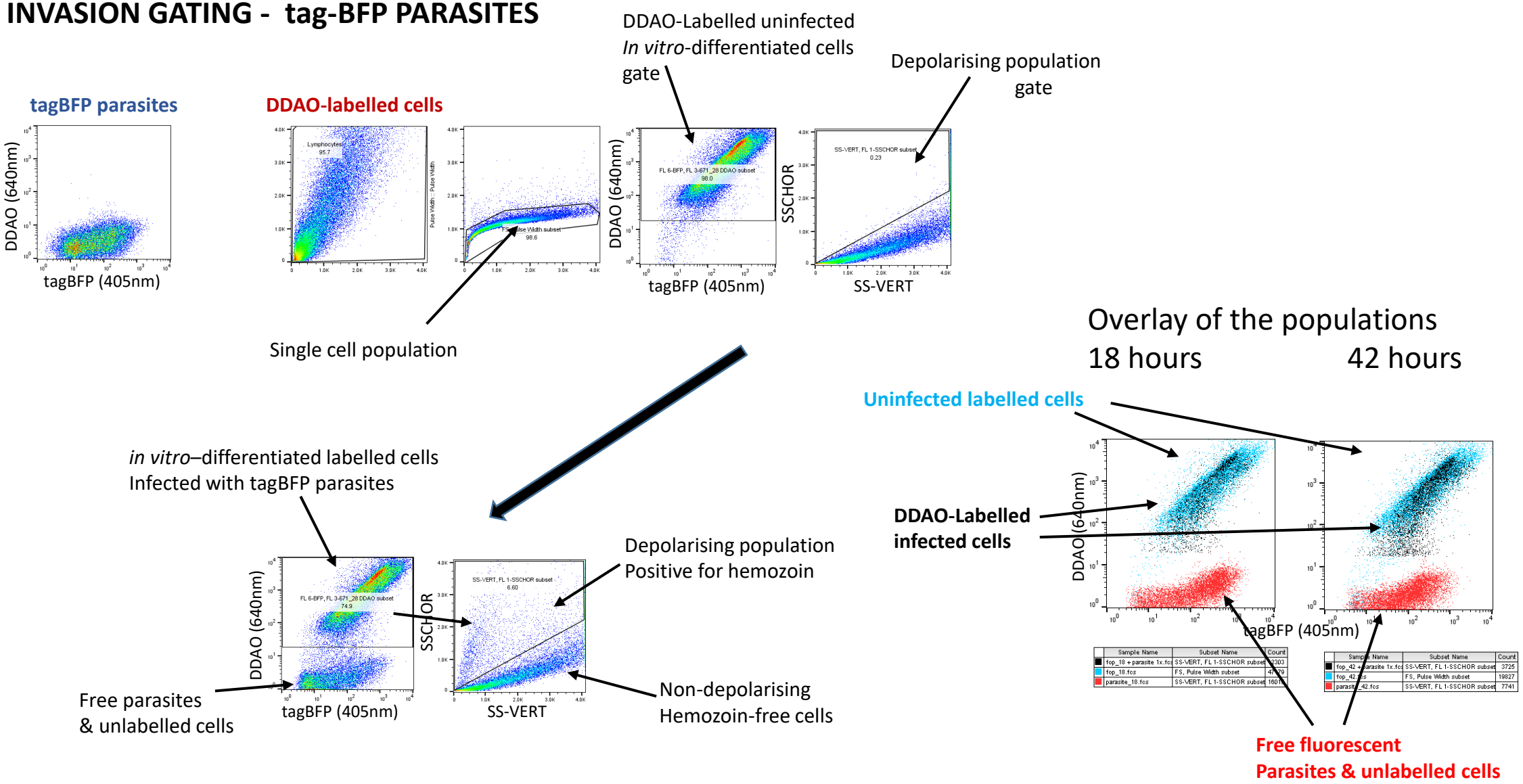
Supplementary Fig 5: gating of invasion assays. A: fluorescent parasites alone; B labelled target cells alone and C depolarisation gate; D co-culture of labelled cells and parasites applying the established gates to assess parasitaemia (E). F overlay of the population of labelled non-infected cells, labelled infected cells and parasites alone.

INVASION GATING - MIDORI-ISHI PARASITES



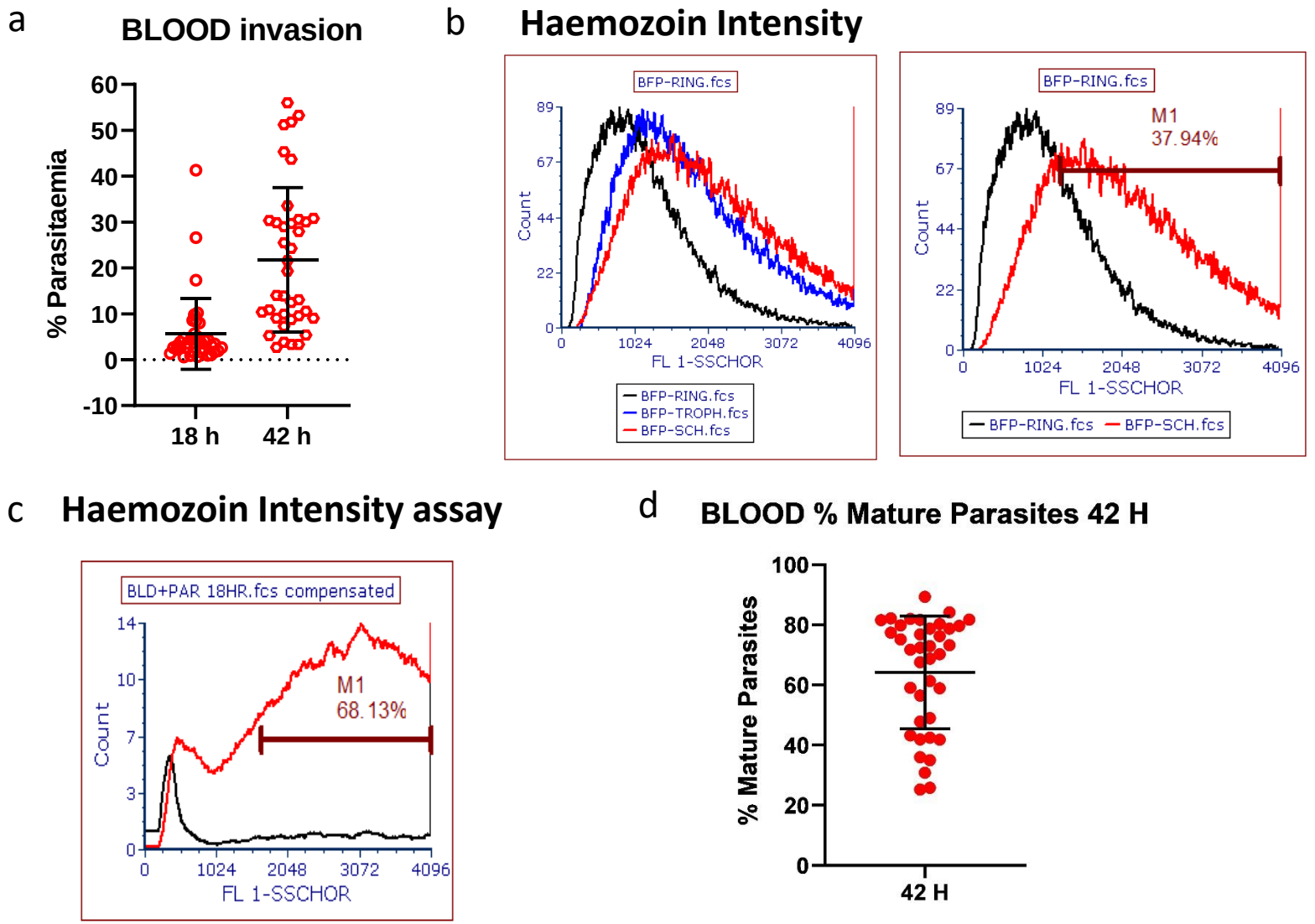
Supplementary Fig 6: gating of invasion assays. Same strategy as Figure 5 but using the far-red cell dye DDAO to label the target cells and parasites expressing Midori-ishi cyan fluorochrome

INVASION GATING - tag-BFP PARASITES



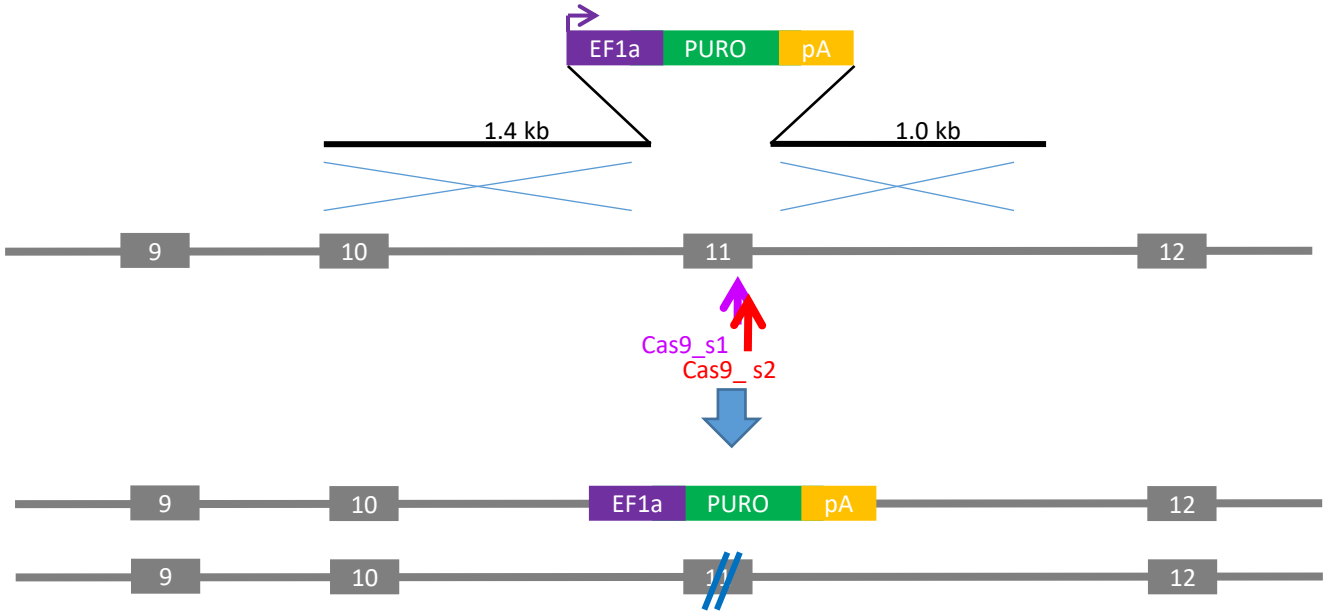
Supplementary Fig 7: gating of invasion assays. Same strategy as Figure 5 but using the far-red cell dye DDAO to label the target cells and parasites expressing tag-BFP fluorochrome

HAEMOZOIN GATE FOR MATURE PARASITES



Supplementary Fig 8: invasion quantification in primary erythrocytes. a: Hz depolarisation of invasion assays at 18 and 42 hours. b: depolarisation intensity in synchronised cultures of parasites. c: determination of Hz intensity gate for assessment of growth. d: % of mature parasites at 42 hours of culture in primary erythrocytes are measured by Hz intensity. Results are presented as means and SD.

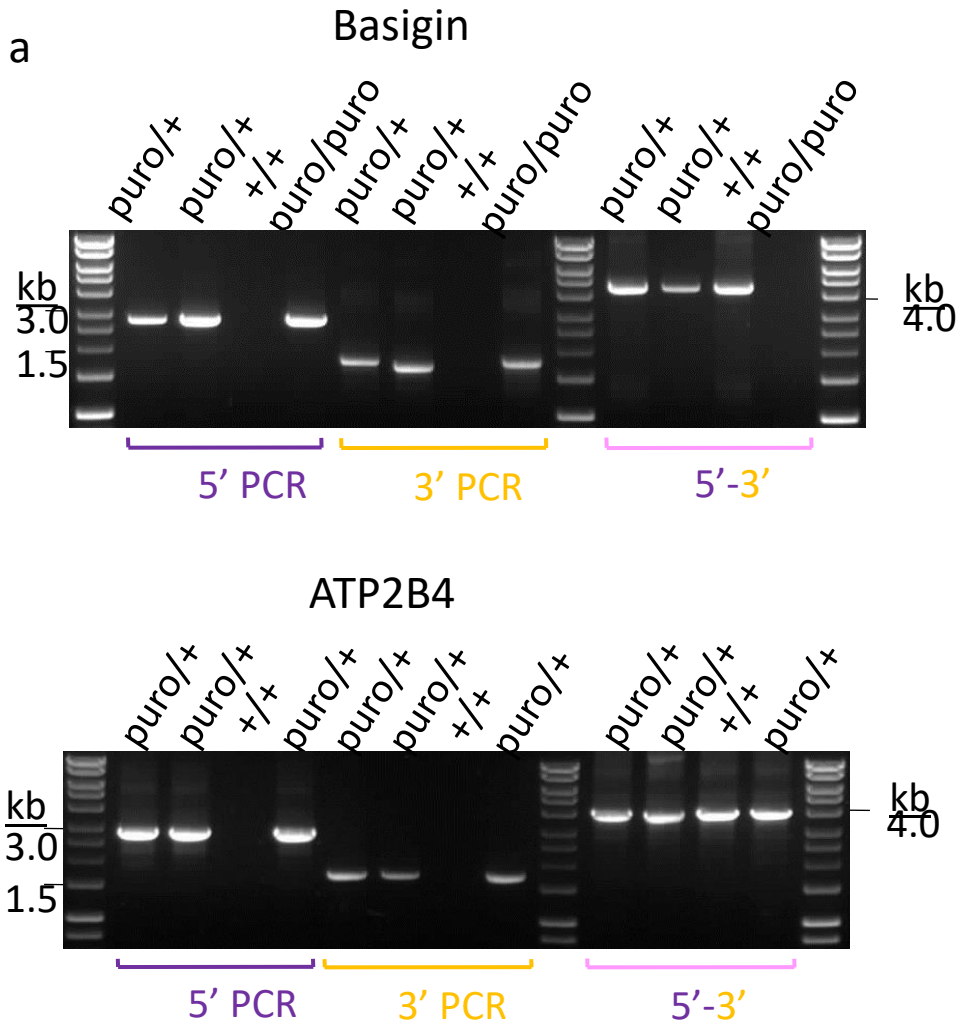
GENOME EDITING STRATEGY



Supplementary Fig 9: diagram of the genome editing strategy used to knock out Basigin and ATP2B4

GENOTYPING OF EDITED LINES

a



b

	…5’ Homology Region		3’ Homology region…
Exon 5	TGG TCT GCA AGT CAG AGT	CCG TGC CAC CTG TCA CTG	ACT GGG CCT GGT A
BSG	TGG TCT GCA AGT CAG AGT	CCG TG- --- --- T CAC TG	A CTG GGC CTG GTA
C5B1	TGG TCT GCA AGT CAG AGT	CCG --- --- -TGT CAC TG	A CTG GGC CTG GTA
B5	TGG TCT GCA AGT CA- ---	--- --- --- C TGT CAC TG	A CTG GGC CTG GTA

	…5’ Homology Region		3’ Homology region…
Exon 11	ATG AGC ACC GTC ATC AGG	AAT CCC AAC GGT GGC TTC	CGT ATG … ATC TGC ATA GCT
ATP2B4 A1	ATG AGC ACC GTC ATC AGG	AAT CCC AAC GGT GC- T TC	GTA TG …A TCT GCA TAG
ATP2B4 E6	ATG AGC ACC GTC ATC AGG	AAT CCC AAC G- T G GCT TC	GTA TG …A TCT GCA TAG

Supplementary Fig 10: assessment of edited cell lines. a: genotyping across the homology arms to detect the insertion of the selection cassette. b: sequencing the second allele to detect damage leading to inactivation.