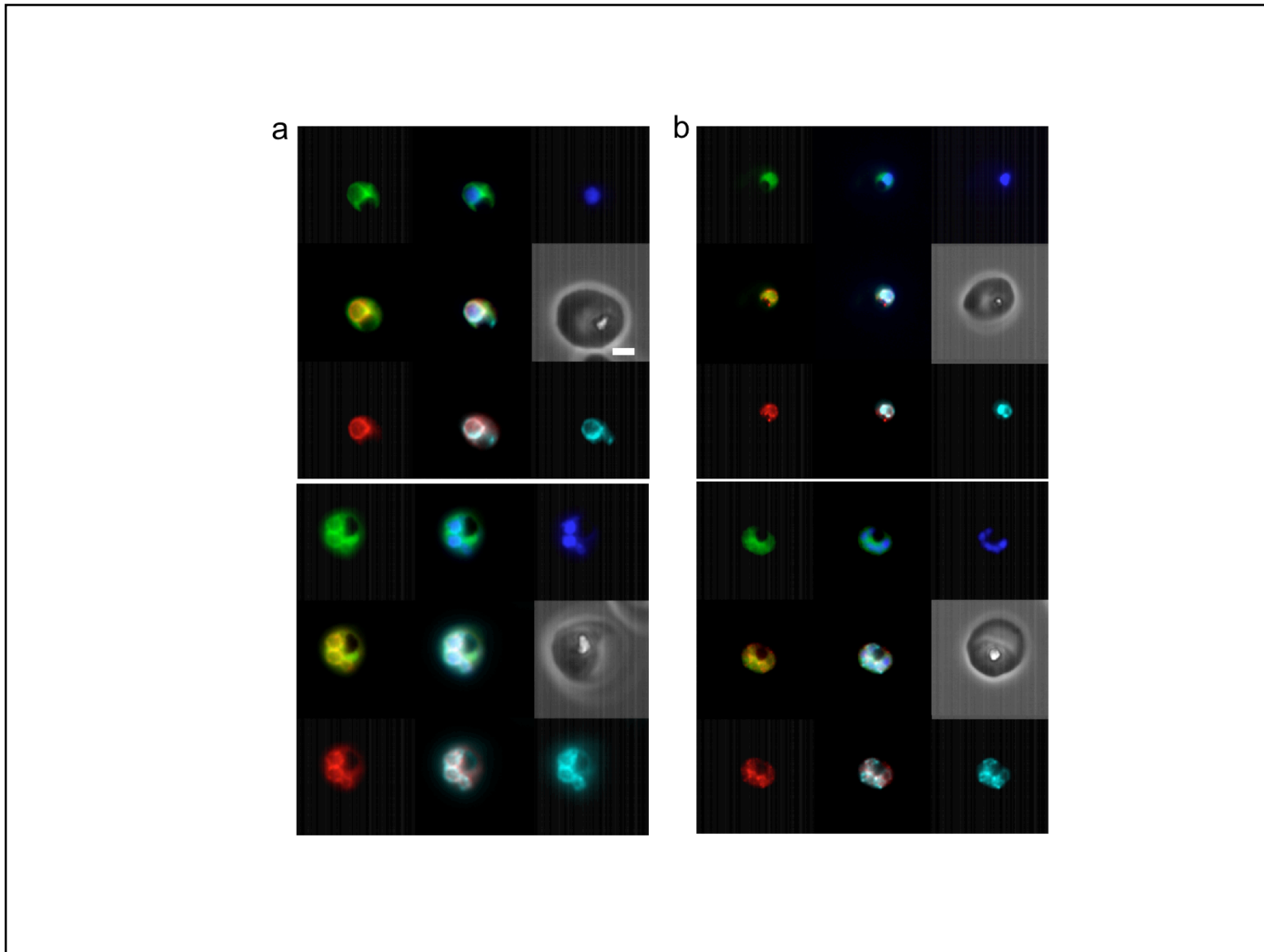
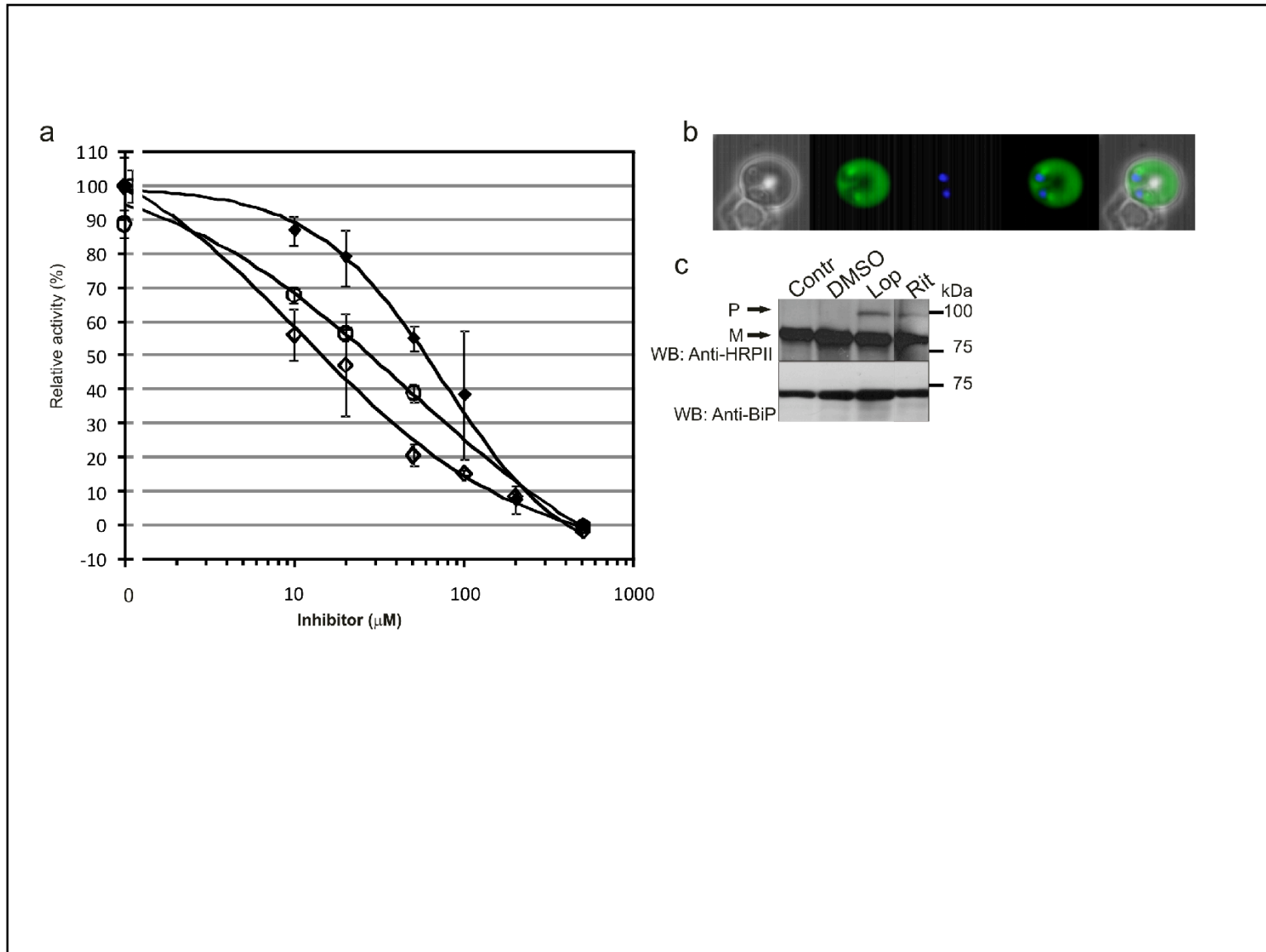


Supplementary Figure 1. Schematic model of exported protein interactions. A PEXEL-containing protein is recognized by PMV in association with chaperones such as HSP 70 and HSP 101. PM V cleaves the PEXEL, releasing mature protein into the stewardship of the chaperones, which usher the protein through the secretory system to the translocon for export into the host erythrocyte.



Supplementary Fig 2. Expression of plasmepsin V in C-terminal fusion lines. a) western blot. Parasite extracts were prepared and assayed using anti- PM V antibody as in Fig. 2. BiP served as loading control. 3D7: parental line; DC6: Full-length fusion; EF2: tail deletion. b,c) Live fluorescence of fusion lines from a). DC6 (b) and EF2 (c). Left to right: Phase, GFP signal, Dapi, fluorescence merge and merge. Bar, 2 μm . d,e) immunofluorescence of fusion lines from a). DC6 (d) and EF2 (e) Parasites were fixed and GFP, anti-PM V (red) and anti-BiP (cyan) signals were detected. Nuclei were imaged with DAPI (blue). Merged images are shown between single channel images and in the center. Phase image is on the right. Bar, 2 microns. Overlap between PM V-GFP and BiP was nearly complete except for a few punctae. These likely represent imaging artifacts since they were seen in the red but not the green channel. Alternatively, they could perhaps represent concentration at ER exit sites (Lee et al., Mol. Micro. 68: 1535-46 (2008)).



Supplementary Figure 3. Effect of aspartic protease inhibitors on activity and protein export. A) inhibition of *in vitro* activity by lopinavir (solid diamonds), ritonavir (open diamonds) and pepstatin (open circles). Error bars indicate the range of triplicate determinations. B) Live fluorescence of histidine-rich protein II (HRP11)-GFP fusion integrant parasites. Mid-trophozoites are shown. Left to right: phase, GFP, DAPI, merges. C) *in vivo* effect on exported protein processing. HRP11-GFP fusion integrant parasites were incubated for 6 h with 50 μM lopinavir, ritonavir or solvent alone, parasite pellets collected and analyzed by western blot using anti-GFP Ab. BiP served as a loading control. Arrows indicate precursor (P) and mature (M) HRP11-GFP. Protease inhibitors: Lopinavir from Kaletra®; Ritonavir from Norvir®; Pepstatin: microbial source from Sigma. The BACE inhibitors BF72 and RP57 (S. Romeo, Milan), BACE inhibitor 1 (Calbiochem) and GRL-8234 (J. Tang, Oklahoma Medical Research Foundation) were all non-inhibitory at high concentrations.

Band #	Mol. Wt. Marker (kDa)	PlasmoDB ID	Description of Protein	PEX= PEXEL Motif or SP= Signal Peptide	# of Peptides found with PMV-wt (α GFP)	# of Peptides found with PMV-mut (α GFP)	# of Peptides found with PMV-wt (α PMV)	Mol. Wt. of Protein, kDa
1	250	PFI1475w	MSP1 Precursor	SP	0	3	2	196.7
		PFE0040c	PfEMP2 or MESA	PEX	0	0	3	168.1
2	150	PF14_0316	DNA topoisomerase II, putative	-	0	3	0	169.9
		PFI1445w	High molecular weight rhoptry protein-2	SP	6	22	13	162.5
3	100	PF14_0201	Surface Protein, Pf113	SP	0	0	3	112.5
		PFI0265c	RhopH3	SP	1	2	3	105.5
		PF11_0175	Heat Shock Protein 101	SP	3	4	5	103
		PF13_0133	Plasmepsin 5-GFP	SP	11	7	0	96.7
		PFL1070c	endoplasmic homolog precursor, putative	SP	6	0	0	95.3
		PF13_0233	myosin A	-	0	4	0	93

		PF07_0029	heat shock protein 86, putative	-	3	4	0	86.7
4	75	PF14_0102	rhoptry-associated protein 1	SP	0	8	2	90.4
		PFL1545c	chaperonin, cpn60	SP	0	2	5	81.7
		PF08_0032	DNAJ protein	-	0	3	0	77
		PF08_0054	Heat shock protein 70	-	2	6	14	74.3
		MAL7P1.228	Heat Shock 70 KDa Protein	-	0	4	7	73.3
		PFI0875w	Heat shock protein 70	SP	4	5	5	72.4
		PF13_0133	Plasmepsin 5	SP	3	0	0	69.4
5	50	MAL8P1.17	Protein disulfide isomerase	SP	0	0	3	55.5
		PF13_0062	Putative Clathrin-adaptor medium chain	-	0	0	4	50.7
		PFD0090c	Plasmodium exported protein (PHISTa)	PEX	0	1	2	50.1
		PF13_0143	phosphoribosylpyrophosphate	-	3	2	3	49.8

			synthetase					
		PF13_0304	elongation factor-1 alpha	-	2	3	4	49.1
		PFE0060w	PIESP2 erythrocyte surface protein	PEX	0	3	5	48.7
		PFE0075c	rhoptry-associated protein 3	SP	0	5	0	47.2
		PFE0080c	rhoptry-associated protein 2	SP	0	7	1	46.9
		PFI1780w	Plasmodium exported protein PHISTc	PEX	0	0	8	45.4
		PFI0880c	glideosome-associated protein 50	SP	3	5	0	44.8
		MAL13P1.237	conserved Plasmodium protein	-	2	3	3	42.4
		PFL2215w	Actin I	-	3	0	3	41.9
		MAL7P1.174	Plasmodium exported protein PHISTb	PEX	0	0	6	37.7
		PF14_0598	glyceraldehyde-3-phosphate dehydrogenase	-	2	0	3	37

		PFE0065w	skeleton-binding protein 1	-	1	2	6	36.4
		PF11_0313	60S Ribosomal protein P0	-	0	0	5	34.9
		PF10_0068	RNA binding protein	-	0	0	3	29.5
		MAL13P1.413	Membrane Associated Histidine Rich Protein (MAHRP-1)	-	0	0	4	28.9

Supplementary Table 1. Proteins identified from the pulldowns in Supplementary Fig. 6. Included are all proteins for which two or more peptides were identified in one of the samples ($p < .05$).