

Supplementary file 2

A network-based approach reveals novel invasion and Maurer's clefts-related proteins in *Plasmodium falciparum*

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Linear link between the expression of genes at RNA and protein level: It is usually assumed that there is a high correlation between RNA expression and proteomic expression. To validate this assumption, we looked at gene-expression of proteins involved in experimentally known key protein-protein interactions. We have observed several valid protein co-expression events for key interaction proteins and complexes relevant to Plasmodium invasion and Maurer's clefts based on both the stage-specific micro array and rna-seq data. Some of our observations are explained below with both co-expression stage and peak gene expression stage information from both the datasets.

Key interactions among invasion-related proteins

1. The success of parasite invasion into host erythrocytes depends on the interactions of parasite surface proteins with the erythrocyte surface proteins. The reticulocyte-binding protein homolog (PF3D7_0424100 – RH5), RH5 interacting protein (PF3D7_0323400 – RIPR) and cysteine-rich protective antigen (PF3D7_0423800 – CyRPA) form a ternary complex and interact with human Basigin [1]. It was observed that RH5, RIPR and CyRPA co-express during the ES (early schizont) and LS (late schizont) stages of IDC from both RNA-seq and DNA microarray data. The peak gene expression stage was found to be late schizont (LS) from both the datasets. Thus after

egress, the concentration of these 3 proteins will be high enough to form a complex required for invasion of the next erythrocyte.

2. After the interactions with host erythrocyte have been established, the parasite forms a moving junction complex composed of apical membrane antigen (PF3D7_1133400 – AMA1) and the rhoptry neck protein 2 (PF3D7_1452000 – RON2) along with RON5 (PF3D7_0817700) and a cAMP-dependent protein kinase (PF3D7_0934800 – PKAc) required for activating the tail domain of AMA1 [2,3]. All 4 proteins were found to be co-expressed at ES and LS stages of both expression datasets. PKAc, RON2 and RON5 had peak gene expression during the ES stage while AMA1 had peak gene expression during the LS stage from both RNA-seq and DNA microarray data. Thus, the corresponding protein concentrations will be sufficient enough for moving junction formation after parasite egress.

3. The glideosome complex is an essential component for parasite invasion composed of myosin A (PF3D7_1342600 - MyoA), myosin A tail domain interacting protein (PF3D7_1246400 – MTIP), actin (PF3D7_1246200 – ACT1), glideosome associated protein 45 (PF3D7_1222700 – GAP45), glideosome associated protein 50 (PF3D7_0918000 – GAP50) and glideosome associated protein 40 (PF3D7_0515700 – GAP40) [3]. All the glideosome components were found to be co-expressed at ES and LS stages from both the expression datasets. GAP50 and GAP40 had peak expression at ES stage while, MyoA, MTIP and ACT1 proteins had peak expression at the LS stage in both the datasets. GAP45 protein had peak gene expression during LS in RNA-seq and ES in DNA microarray data. Thus, in order to facilitate invasion at the beginning of a new life cycle, these proteins are co-expressed at the ES and LS stages which form the glideosome complex after parasite egress.

Also, the calcium-dependent protein kinase 1 (PF3D7_0217500 – CDPK1) which phosphorylates the motor proteins of the glideosome complex was also found to have peak gene expression in the LS stage in both the datasets.

Key interactions among Maurer's clefts-related proteins

1. The parasite has evolved an active vesicular trafficking pathway as already explained in the Results section of the manuscript (Pathway analysis). The coatamer protein II (COPII) vesicle complex is formed by 4 proteins namely: SEC23 (PF3D7_0822600), SEC24A/B (PF3D7_0405100/PF3D7_1361100), SEC13 (PF3D7_1230700) and SEC31 (PF3D7_0214100) [4]. All the proteins were found to be co-expressed at the ER (early ring) stage of both the expression datasets. All the proteins have peak gene expression

during the ER stage of IDC in RNA-seq dataset. Thus, their protein concentrations would be sufficient enough during the ring and trophozoite stages for transporting proteins to Maurer's clefts and to erythrocyte surface.

2. The Plasmodium translocon of exported components (PTEX) is a translocon complex localized at the parasitophorous vacuolar membrane (PVM) for transport of parasite proteins across PVM which is composed of six proteins namely: heat shock protein 101 (PF3D7_1116800 – HSP101), exported protein 2 (PF3D7_1471100 - EXP2), PV protein 1 (PF3D7_1129100 – PV1), thioredoxin 2 (PF3D7_1345100 – TRX2), translocon component 88 (PF3D7_1105600 – PTEX88) and translocon component 150 (PF3D7_1436300 – PTEX150) [5]. From both the expression datasets, all the PTEX proteins were found to be co-expressed at ER, LR, ET and LT stages of IDC. It was observed that, HSP101, TRX2, PTEX88 and PTEX150 had peak gene expression at the LR (late ring) stage while, EXP2 and PV1 had peak gene expression at the LT stage based on RNA-seq data. Thus, the PTEX component proteins were found to co-express during the ring and trophozoite stages of IDC which are the major growth stages where transport is an essential process.

Based on these observations we conclude that, the RNA-seq and DNA microarray datasets used in this study can be considered together as a good estimate for co-expression of interacting proteins. Since co-expression is the major criteria for protein-protein interactions, the assumption of a linear link between mRNA counts and protein abundance can be considered valid based on our results.

Table S1: The gene counts for different number of stages where the expression data is derived from both datasets or only from either DNA microarray or RNA-seq dataset.

| No. of stages | Data from both datasets | Data only from DNA microarray | Data only from RNA-seq |
|----------------------|--------------------------------|--------------------------------------|-------------------------------|
| 1 | 560 | 226 | 118 |
| 2 | 505 | 135 | 98 |
| 3 | 437 | 149 | 71 |
| 4 | 490 | 134 | 69 |
| 5 | 300 | 100 | 43 |
| 6 | 773 | 82 | 67 |
| 7 | 0 | 143 | 0 |
| Total | 3065 | 969 | 466 |

Table S1: The gene counts for different number of stages where the expression data is derived from both datasets or only from either DNA microarray or RNA-seq dataset. Apart from these, both dataset show gene-expression for 135 genes but they does not overlap with any common stage.

Table S2: RWR seed and predicted major families of proteins related to invasion. In Table 2 of the main manuscript short names are provided.

| Type | Gene ID | Protein name | Seed/Predicted |
|---------------------------|---------------|--|----------------|
| Microneme proteins | PF3D7_0323400 | Rh5 interacting protein (RIPR) | SEED |
| | PF3D7_0102500 | erythrocyte binding antigen-181 (EBA181) | SEED |
| | PF3D7_0731500 | erythrocyte binding antigen-175 (EBA175) | SEED |
| | PF3D7_1301600 | erythrocyte binding antigen-140 (EBA140) | SEED |
| | PF3D7_1028700 | merozoite TRAP-like protein (MTRAP) | SEED |
| | PF3D7_1136900 | Subtilisin-like protease 2 (SUB2) | PREDICTED |
| | PF3D7_0423800 | Cysteine-rich protective antigen (CyRPA) | PREDICTED |
| | PF3D7_0316000 | Microneme associated antigen (MA) | PREDICTED |
| | PF3D7_0212600 | Secreted protein with altered thrombospondin repeat domain (SPATR) | PREDICTED |
| | PF3D7_0414900 | Armadillo repeat-containing rhoptry protein (ARO) | PREDICTED |
| | PF3D7_0828800 | GPI-anchored micronemal antigen (GAMA) | PREDICTED |
| Rhoptry proteins | PF3D7_0817700 | rhoptry neck protein 5 (RON5) | SEED |
| | PF3D7_1452000 | rhoptry neck protein 2 (RON2) | SEED |
| | PF3D7_0424100 | reticulocyte binding protein homologue 5 (RH5) | SEED |
| | PF3D7_0424200 | reticulocyte binding protein homologue 4 (RH4) | SEED |
| | PF3D7_0402300 | reticulocyte binding protein homologue 1 (RH1) | SEED |
| | PF3D7_0302200 | Cytoadherence-linked asexual protein 3.2 (CLAG3.2) | PREDICTED |
| | PF3D7_1218000 | Thrombospondin-related apical membrane protein (TRAMP) | PREDICTED |
| | PF3D7_1410400 | Rhoptry-associated protein 1 (RAP1) | PREDICTED |
| | PF3D7_0722200 | Rhoptry-associated leucine-zipper like protein 1 (RALP1) | PREDICTED |
| | PF3D7_0613300 | Rhoptry protein ROP14 (ROP14) | PREDICTED |
| | PF3D7_0214900 | Rhoptry neck protein 6 (RON6) | PREDICTED |
| | PF3D7_0405900 | Apical sushi protein (ASP) | PREDICTED |

| | | | |
|--|---------------|--|-----------|
| | PF3D7_0501600 | Rhoptry-associated protein 2 (RAP2) | PREDICTED |
| | PF3D7_0212600 | Secreted protein with altered thrombospondin repeat domain (SPATR) | PREDICTED |
| | PF3D7_0528400 | Palmitoyl transferase (DHHC7) | PREDICTED |
| | PF3D7_0501500 | Rhoptry-associated protein 3 (RAP3) | PREDICTED |
| | PF3D7_1017100 | Rhoptry neck protein 12 (RON12) | PREDICTED |
| | PF3D7_0929400 | High molecular weight rhoptry protein 2 (RhopH2) | PREDICTED |
| | PF3D7_0905400 | High molecular weight rhoptry protein 3 (RhopH3) | PREDICTED |
| | PF3D7_0707300 | Rhoptry associated membrane antigen (RAMA) | PREDICTED |
| | PF3D7_0220800 | Cytoadherence-linked asexual protein 2 (CLAG2) | PREDICTED |
| | PF3D7_0419700 | Apical merozoite protein (Pf34) | PREDICTED |
| | PF3D7_1351700 | Inner membrane complex protein 1f, putative (IMC1f) | PREDICTED |
| | PF3D7_0302500 | Cytoadherence-linked asexual protein 3.1 (CLAG3.1) | PREDICTED |
| | PF3D7_0109000 | Photosensitized INA-labeled protein PHIL1, putative (PHIL1) | PREDICTED |
| Inner membrane complex proteins | PF3D7_0525800 | Inner membrane complex protein 1g, putative (IMC1g) | PREDICTED |
| | PF3D7_1003600 | Inner membrane complex protein 1c, putative (IMC1c) | PREDICTED |
| | PF3D7_0304100 | Inner membrane complex protein 1e, putative (IMC1e) | PREDICTED |
| | PF3D7_1222700 | Glideosome-associated protein 45 (GAP45) | PREDICTED |
| | PF3D7_1246400 | Myosin A tail domain interacting protein (MTIP) | PREDICTED |
| | PF3D7_1323700 | Glideosome associated protein with multiple membrane spans 1 (GAPM1) | PREDICTED |
| | PF3D7_0423500 | Glideosome associated protein with multiple membrane spans 2 (GAPM2) | PREDICTED |
| | PF3D7_1406800 | Glideosome associated protein with multiple membrane spans 3 (GAPM3) | PREDICTED |
| | PF3D7_0515700 | Glideosome-associated protein 40 (GAP40) | PREDICTED |

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| | PF3D7_0918000 | Glideosome-associated protein 50 (GAP50) | PREDICTED |
| | PF3D7_1460600 | Inner membrane complex sub-compartment protein 3 (ISP3) | PREDICTED |
| | PF3D7_1341500 | Inner membrane complex suture component, putative (ISC1) | PREDICTED |
| | PF3D7_1345600 | Inner membrane complex protein | PREDICTED |
| | PF3D7_0522600 | Inner membrane complex protein | PREDICTED |
| | PF3D7_0805200 | Gamete release protein, putative (GAMER) | PREDICTED |
| | PF3D7_1342600 | Myosin A (MyoA) | PREDICTED |
| | PF3D7_1246400 | Myosin A tail domain interacting protein (MTIP) | PREDICTED |
| | PF3D7_0828800 | GPI-anchored micronemal antigen (GAMA) | PREDICTED |
| | PF3D7_0405900 | Apical sushi protein (ASP) | PREDICTED |
| Attachment of GPI anchor to protein | PF3D7_0930300 | merozoite surface protein 1 (MSP1) | SEED |
| | PF3D7_0620400 | Merozoite surface protein 10 (MSP10) | PREDICTED |
| | PF3D7_0206800 | Merozoite surface protein 2 (MSP2) | PREDICTED |
| | PF3D7_0707300 | Rhoptry-associated membrane antigen (RAMA) | PREDICTED |
| | PF3D7_0508000 | 6-cysteine protein (P38) | PREDICTED |
| | PF3D7_0612700 | 6-cysteine protein (P12) | PREDICTED |
| | PF3D7_0419700 | Apical merozoite protein (Pf34) | PREDICTED |
| | PF3D7_1136200 | Conserved Plasmodium protein unknown function | PREDICTED |
| | PF3D7_1036000 | Merozoite surface protein 11 (MSP11) | PREDICTED |
| | PF3D7_1035300 | Glutamate-rich protein (GLURP) | PREDICTED |
| Merozoite and other surface proteins | PF3D7_1335100 | merozoite surface protein 7 (MSP7) | SEED |
| | PF3D7_1035500 | merozoite surface protein 6 (MSP6) | SEED |
| | PF3D7_1028700 | merozoite TRAP-like protein (MTRAP) | SEED |
| | PF3D7_0930300 | merozoite surface protein 1 (MSP1) | SEED |
| | PF3D7_1035900 | Probable protein, unknown function (M566) | PREDICTED |
| | PF3D7_1035400 | Merozoite surface protein 3 (MSP3) | PREDICTED |
| | PF3D7_1035700 | Duffy-binding like merozoite surface protein (DBLMSP) | PREDICTED |
| | PF3D7_1228600 | Merozoite surface protein 9 (MSP9) | PREDICTED |
| | PF3D7_0207000 | Merozoite surface protein 4 (MSP4) | PREDICTED |

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| | PF3D7_1036300 | Merozoite surface protein (DBLMSP2) | PREDICTED |
| | PF3D7_1334800 | MSP7-like protein (MSRP2) | PREDICTED |
| | PF3D7_0620400 | Merozoite surface protein 10 (MSP10) | PREDICTED |
| | PF3D7_0206800 | Merozoite surface protein 2 (MSP2) | PREDICTED |
| | PF3D7_0207000 | Merozoite surface protein 4 (MSP4) | PREDICTED |
| | PF3D7_1228600 | Merozoite surface protein 9 (MSP9) | PREDICTED |
| | PF3D7_1035600 | Merozoite surface protein (H101) | PREDICTED |
| | PF3D7_0419700 | Apical merozoite protein (Pf34) | PREDICTED |
| | PF3D7_0507500 | Subtilisin-like protease 1 (SUB1) | PREDICTED |
| | PF3D7_1136900 | Subtilisin-like protease 2 (SUB2) | PREDICTED |
| | | | |
| Merozoite dense granule proteins | PF3D7_0102200 | Ring-infected erythrocyte surface antigen (RESA) | PREDICTED |
| | PF3D7_1149200 | Ring-infected erythrocyte surface antigen (RESA) | PREDICTED |
| | PF3D7_0503400 | Actin depolymerising factor 1 (ADF1) | PREDICTED |
| | PF3D7_1361400 | Actin depolymerising factor 2 (ADF2) | PREDICTED |
| Actin binding/motor activity | PF3D7_1251200 | Coronin | PREDICTED |
| | PF3D7_0932200 | Profilin, putative (PFN) | PREDICTED |
| | PF3D7_1126700 | Autophagy-related protein 23, putative (ATG23) | PREDICTED |
| | PF3D7_1229800 | Myosin D (MyoD) | PREDICTED |
| | PF3D7_1342600 | Myosin A (MyoA) | PREDICTED |
| | PF3D7_0613900 | Myosin E (MyoE) | PREDICTED |
| | PF3D7_0503600 | Myosin B (MyoB) | PREDICTED |
| | PF3D7_1118700 | Myosin light chain B (MLC-B) | PREDICTED |
| | PF3D7_1246200 | Actin 1 (ACT1) | PREDICTED |
| | PF3D7_1037500 | Dynamin-like protein 2 (DYN2) | PREDICTED |
| | PF3D7_0508900 | Conserved Plasmodium protein, unknown function | PREDICTED |
| | PF3D7_1435600 | Conserved Plasmodium protein, unknown function | PREDICTED |
| | PF3D7_1320700 | Conserved Plasmodium protein, unknown function | PREDICTED |
| | PF3D7_1003400 | Conserved Plasmodium protein, unknown function | PREDICTED |

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| | PF3D7_1327300 | Conserved Plasmodium protein, unknown function | PREDICTED |
| | PF3D7_1206300 | Conserved Plasmodium protein, unknown function | PREDICTED |
| | PF3D7_0214600 | Serine/threonine protein kinase, putative | PREDICTED |
| | PF3D7_1337800 | Calcium-dependent protein kinase 5 (CDPK5) | PREDICTED |
| Kinases | PF3D7_1104900 | Calcium/calmodulin-dependent protein kinase | PREDICTED |
| | PF3D7_0217500 | Calcium-dependent protein kinase 1 (CDPK1) | PREDICTED |
| | PF3D7_1356800 | Serine/threonine protein kinase, putative (ARK3) | PREDICTED |
| | PF3D7_1238900 | Protein kinase 2 (PK2) | PREDICTED |
| | PF3D7_1436600 | cGMP-dependent protein kinase (PKG) | PREDICTED |
| | PF3D7_0717500 | Calcium-dependent protein kinase 4 (CDPK4) | PREDICTED |
| | PF3D7_1223100 | cAMP-dependent protein kinase regulatory subunit (PKAr) | PREDICTED |
| | PF3D7_0934800 | cAMP-dependent protein kinase catalytic subunit (PKAc) | PREDICTED |
| | PF3D7_0507500 | Subtilisin-like protease 1 (SUB1) | PREDICTED |
| | PF3D7_1136900 | Subtilisin-like protease 2 (SUB2) | PREDICTED |
| Proteolysis | PF3D7_0507200 | Subtilisin-like protease 3 (SUB3) | PREDICTED |
| | PF3D7_0808200 | Plasmepsin X | PREDICTED |
| | PF3D7_1430200 | Plasmepsin IX | PREDICTED |
| | PF3D7_0404700 | Dipeptidyl aminopeptidase 3 (DPAP3) | PREDICTED |
| | PF3D7_0506900 | Rhomboid protease 4 (ROM4) | PREDICTED |
| | PF3D7_0207800 | Serine repeat antigen 3 (SERA3) | PREDICTED |
| | PF3D7_0207700 | Serine repeat antigen 4 (SERA4) | PREDICTED |
| | PF3D7_0207600 | Serine repeat antigen 5 (SERA5) | PREDICTED |
| | PF3D7_1308000 | Conserved Plasmodium protein, unknown function | PREDICTED |

Table S3. RWR seed and predicted major families of proteins related to Maurer's clefts. In Table 4 of the main manuscript short names are provided.

| Type | GeneID | Description | Seed/Predicted |
|-------------------------------------|-----------------|--|-----------------------|
| Vesicular transport proteins | PF3D7_0822600 | protein transport protein SEC23 (SEC23) | SEED |
| | PF3D7_0214100 | protein transport protein SEC31 (SEC31) | SEED |
| | PF3D7_1437800 | trafficking protein particle complex subunit 5, putative (TRAPPC5) | SEED |
| | PF3D7_0416800 | small GTP-binding protein sar1 (SAR1) | SEED |
| | PF3D7_0303000 | N-ethylmaleimide-sensitive fusion protein (NSF) | SEED |
| | PF3D7_1230700 | protein transport protein SEC13 (SEC13) | PREDICTED |
| | PF3D7_0320100 | protein transport protein SEC22 (SEC22) | PREDICTED |
| | PF3D7_1361100 | protein transport protein Sec24A (SEC24A) | PREDICTED |
| | PF3D7_0405100 | protein transport protein Sec24B (SEC24B) | PREDICTED |
| | PF3D7_1332300 | trafficking protein particle complex subunit 2, putative (TRAPPC2) | PREDICTED |
| | PF3D7_0418500 | trafficking protein particle complex subunit 3, putative (BET3) | PREDICTED |
| | PF3D7_0512600 | ras-related protein Rab-1B (RAB1b) | PREDICTED |
| | PF3D7_0310700 | trafficking protein particle complex subunit 4, putative | PREDICTED |
| | PF3D7_0618700 | trafficking protein particle complex subunit 6A, putative | PREDICTED |
| Heat shock proteins | PF3D7_0501100.2 | heat shock protein 40, type II (HSP40) | SEED |
| | PF3D7_0917900 | heat shock protein 70 (HSP70-2) | SEED |
| | PF3D7_1134000 | heat shock protein 70 (HSP70-3) | SEED |
| | PF3D7_0818900 | heat shock protein 70 (HSP70) | SEED |
| | PF3D7_0708400 | heat shock protein 90 (HSP90) | SEED |
| | PF3D7_0827900 | protein disulfide isomerase (PDI8) | SEED |
| | PF3D7_0102200 | ring-infected erythrocyte surface antigen (RESA) | SEED |
| | PF3D7_0201600 | PHISTb domain-containing RESA-like protein 1 (RLP1) | SEED |

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| | PF3D7_1222300 | endoplasmin, putative (GRP94) | SEED |
| | PF3D7_1116800 | heat shock protein 101 (HSP101) | PREDICTED |
| | PF3D7_0113700 | heat shock protein 40, type II (HSP40) | PREDICTED |
| | PF3D7_1015600 | heat shock protein 60 (HSP60) | PREDICTED |
| | PF3D7_1211400 | heat shock protein DNAJ homologue Pfj4 (PflJ4) | PREDICTED |
| | PF3D7_0201800 | knob associated heat shock protein 40 (KAHsp40) | PREDICTED |
| | PF3D7_0213100 | protein SIS1 (SIS1) | PREDICTED |
| | PF3D7_0322000 | peptidyl-prolyl cis-trans isomerase (CYP19A) | PREDICTED |
| | PF3D7_1211400 | heat shock protein DNAJ homologue Pfj4 (PflJ4) | PREDICTED |
| | PF3D7_1149200 | ring-infected erythrocyte surface antigen (RESA) | PREDICTED |
| | PF3D7_1473200 | DnaJ protein, putative | PREDICTED |
| | PF3D7_1401100 | DnaJ protein, putative | PREDICTED |
| | PF3D7_1149600 | DnaJ protein, putative | PREDICTED |
| | PF3D7_0220100 | DnaJ protein, putative | PREDICTED |
| | PF3D7_0201700 | DnaJ protein, putative | PREDICTED |
| Kinases | PF3D7_1008900 | adenylate kinase (AK1) | SEED |
| | PF3D7_0312400 | glycogen synthase kinase 3 (GSK3) | SEED |
| | PF3D7_0626800 | pyruvate kinase (PyrK) | SEED |
| | PF3D7_0826700 | receptor for activated c kinase (RACK) | SEED |
| | PF3D7_1401800 | choline kinase (CK) | PREDICTED |
| | PF3D7_1124600 | ethanolamine kinase (EK) | PREDICTED |
| | PF3D7_1351600 | glycerol kinase (GK) | PREDICTED |
| | PF3D7_0624000 | hexokinase (HK) | PREDICTED |
| | PF3D7_0922500 | phosphoglycerate kinase (PGK) | PREDICTED |
| | PF3D7_1443000 | serine/threonine protein kinase (SRPK2) | PREDICTED |
| | PF3D7_1016400 | serine/threonine protein kinase, FIKK family (FIKK10.1) | PREDICTED |
| | PF3D7_1039000 | serine/threonine protein kinase, FIKK family (FIKK10.2) | PREDICTED |
| | PF3D7_0424500 | serine/threonine protein kinase, FIKK family | PREDICTED |

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| | | (FIKK4.1) | |
| | PF3D7_0424700 | serine/threonine protein kinase, FIKK family (FIKK4.2) | PREDICTED |
| Proteins involved in Metabolism | PF3D7_1479000 | acyl-CoA synthetase (ACS1a) | SEED |
| | PF3D7_1462800 | glyceraldehyde-3-phosphate dehydrogenase (GAPDH) | SEED |
| | PF3D7_1012400 | hypoxanthine-guanine phosphoribosyltransferase (HGPRT) | SEED |
| | PF3D7_1008900 | adenylate kinase (AK1) | SEED |
| | PF3D7_0312400 | glycogen synthase kinase 3 (GSK3) | SEED |
| | PF3D7_1324900 | L-lactate dehydrogenase (LDH) | SEED |
| | PF3D7_1343000 | phosphoethanolamine N-methyltransferase (PMT) | SEED |
| | PF3D7_0513300 | purine nucleoside phosphorylase (PNP) | SEED |
| | PF3D7_0626800 | pyruvate kinase (PyrK) | SEED |
| | PF3D7_1439900 | triosephosphate isomerase (TIM) | SEED |
| | PF3D7_0525100 | acyl-CoA synthetase (ACS10) | PREDICTED |
| | PF3D7_1253400 | acyl-CoA synthetase (ACS3) | PREDICTED |
| | PF3D7_0401900 | acyl-CoA synthetase (ACS6) | PREDICTED |
| | PF3D7_1200700 | acyl-CoA synthetase (ACS7) | PREDICTED |
| | PF3D7_1029600 | adenosine deaminase (ADA) | PREDICTED |
| | PF3D7_1436000 | glucose-6-phosphate isomerase (GPI) | PREDICTED |
| | PF3D7_1252600 | lysophospholipase, putative | PREDICTED |
| | PF3D7_1351600 | glycerol kinase (GK) | PREDICTED |
| | PF3D7_0624000 | hexokinase (HK) | PREDICTED |
| | PF3D7_1347200 | nucleoside transporter 1 (NT1) | PREDICTED |
| | PF3D7_0922500 | phosphoglycerate kinase (PGK) | PREDICTED |
| | PF3D7_1120100 | phosphoglycerate mutase, putative (PGM1) | PREDICTED |
| | PF3D7_0520900 | S-adenosyl-L-homocysteine hydrolase (SAHH) | PREDICTED |
| | PF3D7_0922200 | S-adenosylmethionine synthetase (SAMS) | PREDICTED |
| | PF3D7_1438900 | thioredoxin peroxidase 1 (Trx-Px1) | PREDICTED |
| | PF3D7_0610800 | transketolase (TK) | PREDICTED |
| | PF3D7_0219500 | pseudouridine synthase, putative | PREDICTED |

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|---|---------------|---|-----------|
| | PF3D7_0914000 | pseudouridylate synthase, putative | PREDICTED |
| | PF3D7_1432700 | protein-L-isoaspartate(D-aspartate) O-methyltransferase, putative | PREDICTED |
| | PF3D7_1124000 | endoplasmic reticulum oxidoreductin, putative (ERO1) | PREDICTED |
| | PF3D7_1029600 | adenosine deaminase (ADA) | PREDICTED |
| | PF3D7_0206700 | adenylosuccinate lyase (ASL) | PREDICTED |
| | PF3D7_1001400 | alpha/beta hydrolase, putative | PREDICTED |
| | PF3D7_1322000 | adenosine-diphosphatase, putative | PREDICTED |
| Proteins involved in PfEMP1 export | PF3D7_0202200 | EMP1-trafficking protein (PTP1) | SEED |
| | PF3D7_0731100 | EMP1-trafficking protein (PTP2) | SEED |
| | PF3D7_1478600 | EMP1-trafficking protein (PTP3) | SEED |
| | PF3D7_0730900 | EMP1-trafficking protein (PTP4) | SEED |
| | PF3D7_1002100 | EMP1-trafficking protein (PTP5) | SEED |
| | PF3D7_1302000 | EMP1-trafficking protein (PTP6) | SEED |
| | PF3D7_0201900 | erythrocyte membrane protein 3 (EMP3) | SEED |
| | PF3D7_1471100 | exported protein 2 (EXP2) | SEED |
| | PF3D7_0202000 | knob-associated histidine-rich protein (KAHRP) | SEED |
| | PF3D7_1370300 | membrane associated histidine-rich protein (MAHRP1) | SEED |
| | PF3D7_1353200 | membrane associated histidine-rich protein (MAHRP2) | SEED |
| | PF3D7_0935900 | ring-exported protein 1 (REX1) | SEED |
| | PF3D7_0936300 | ring-exported protein 3 (REX3) | SEED |
| | PF3D7_0936400 | ring-exported protein 4 (REX4) | SEED |
| | PF3D7_0102200 | ring-infected erythrocyte surface antigen (RESA) | SEED |
| | PF3D7_0501300 | skeleton-binding protein 1 (SBP1) | SEED |
| | PF3D7_0702400 | small exported membrane protein 1 (SEMP1) | SEED |
| | PF3D7_0201600 | PHISTb domain-containing RESA-like protein 1 (RLP1) | SEED |
| | PF3D7_1101900 | erythrocyte membrane protein 1 (PfEMP1), truncated, pseudogene | PREDICTED |
| | PF3D7_1200600 | erythrocyte membrane protein 1, PfEMP1 | PREDICTED |

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| | | (VAR2CSA) | |
| | PF3D7_1116800 | heat shock protein 101 (HSP101) | PREDICTED |
| | PF3D7_0831800 | histidine-rich protein II (HRPII) | PREDICTED |
| | PF3D7_1372200 | histidine-rich protein III (HRPIII) | PREDICTED |
| | PF3D7_0201800 | knob associated heat shock protein 40 (KAHsp40) | PREDICTED |
| | PF3D7_1149200 | ring-infected erythrocyte surface antigen | PREDICTED |
| Exported proteins | PF3D7_1121600 | exported protein 1 (EXP1) | SEED |
| | PF3D7_0310400 | parasite-infected erythrocyte surface protein (PIESP1) | SEED |
| | PF3D7_0401800 | Plasmodium exported protein (PHISTb), unknown function (PfD80) | SEED |
| | PF3D7_0424600 | Plasmodium exported protein (PHISTb), unknown function | SEED |
| | PF3D7_0501000 | Plasmodium exported protein, unknown function | SEED |
| | PF3D7_0501200 | parasite-infected erythrocyte surface protein (PIESP2) | SEED |
| | PF3D7_0532300 | Plasmodium exported protein (PHISTb), unknown function | SEED |
| | PF3D7_0603400 | trophozoite exported protein 1 (TEX1) | SEED |
| | PF3D7_0631500 | exported protein family 3 (EPF3) | SEED |
| | PF3D7_0702100 | Plasmodium exported protein (PHISTb), unknown function, pseudogene | SEED |
| | PF3D7_0702400 | small exported membrane protein 1 (SEMP1) | SEED |
| | PF3D7_0731300 | Plasmodium exported protein (PHISTb), unknown function (PfG174) | SEED |
| | PF3D7_0935900 | ring-exported protein 1 (REX1) | SEED |
| | PF3D7_0936300 | ring-exported protein 3 (REX3) | SEED |
| | PF3D7_0936400 | ring-exported protein 4 (REX4) | SEED |
| | PF3D7_1001000 | Plasmodium exported protein (hyp12), unknown function (PfJ13) | SEED |
| | PF3D7_1001900 | Plasmodium exported protein (hyp16), unknown function (PfJ23) | SEED |
| | PF3D7_1101500 | exported protein family 4 (EPF4) | SEED |
| | PF3D7_1201000 | Plasmodium exported protein (PHISTb), | SEED |

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| | | unknown function | |
| | PF3D7_1471100 | exported protein 2 (EXP2) | SEED |
| | PF3D7_0112900 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0201500 | Plasmodium exported protein (hyp9), unknown function | PREDICTED |
| | PF3D7_0202300 | Plasmodium exported protein (hyp11), unknown function | PREDICTED |
| | PF3D7_0219700 | Plasmodium exported protein (PHISTc), unknown function (GEXP20) | PREDICTED |
| | PF3D7_0220200 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0221700 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0301600 | Plasmodium exported protein (hyp1), unknown function (GEXP21) | PREDICTED |
| | PF3D7_0301800 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0402000 | Plasmodium exported protein (PHISTa), unknown function | PREDICTED |
| | PF3D7_0402100 | Plasmodium exported protein (PHISTb), unknown function | PREDICTED |
| | PF3D7_0424000 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_0532600 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0701900 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0702000 | Plasmodium exported protein (hyp12), unknown function | PREDICTED |
| | PF3D7_0726100 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0730800.2 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0731200 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0800900 | Plasmodium exported protein (hyp7), unknown function, pseudogene | PREDICTED |

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| | PF3D7_0801000 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_0830600 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_0935500 | Plasmodium exported protein, unknown function (GEXP22) | PREDICTED |
| | PF3D7_0935700 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_0936200 | Plasmodium exported protein (hyp11), unknown function | PREDICTED |
| | PF3D7_0936600 | Plasmodium exported protein (PHISTc), unknown function (GEXP05) | PREDICTED |
| | PF3D7_0936800 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_1016700 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_1016800 | Plasmodium exported protein (PHISTc), unknown function | PREDICTED |
| | PF3D7_1148700 | Plasmodium exported protein (PHISTc), unknown function (GEXP12) | PREDICTED |
| | PF3D7_1148900 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_1201200 | Plasmodium exported protein (PHISTa-like), unknown function | PREDICTED |
| | PF3D7_1252900 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_1253100 | Plasmodium exported protein (PHISTa), unknown function | PREDICTED |
| | PF3D7_1253300 | Plasmodium exported protein (PHISTa), unknown function, pseudogene | PREDICTED |
| | PF3D7_1301400 | Plasmodium exported protein (hyp12), unknown function (HYP12) | PREDICTED |
| | PF3D7_1301700 | Plasmodium exported protein (hyp8), unknown function (GEXP07) | PREDICTED |
| | PF3D7_1352900 | Plasmodium exported protein, unknown function | PREDICTED |
| | PF3D7_1401200 | Plasmodium exported protein, unknown function | PREDICTED |

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| | PF3D7_1476200 | Plasmodium exported protein (PHISTb), unknown function | PREDICTED |
| | PF3D7_1478000 | Plasmodium exported protein (PHISTa), unknown function (GEXP17) | PREDICTED |
| | PF3D7_1478800 | Plasmodium exported protein, unknown function | PREDICTED |
| Gametocyte- specific proteins | PF3D7_1038400 | gametocyte-specific protein (Pf11-1) | SEED |
| | PF3D7_0935600 | gametocytogenesis-implicated protein (GIG) | PREDICTED |

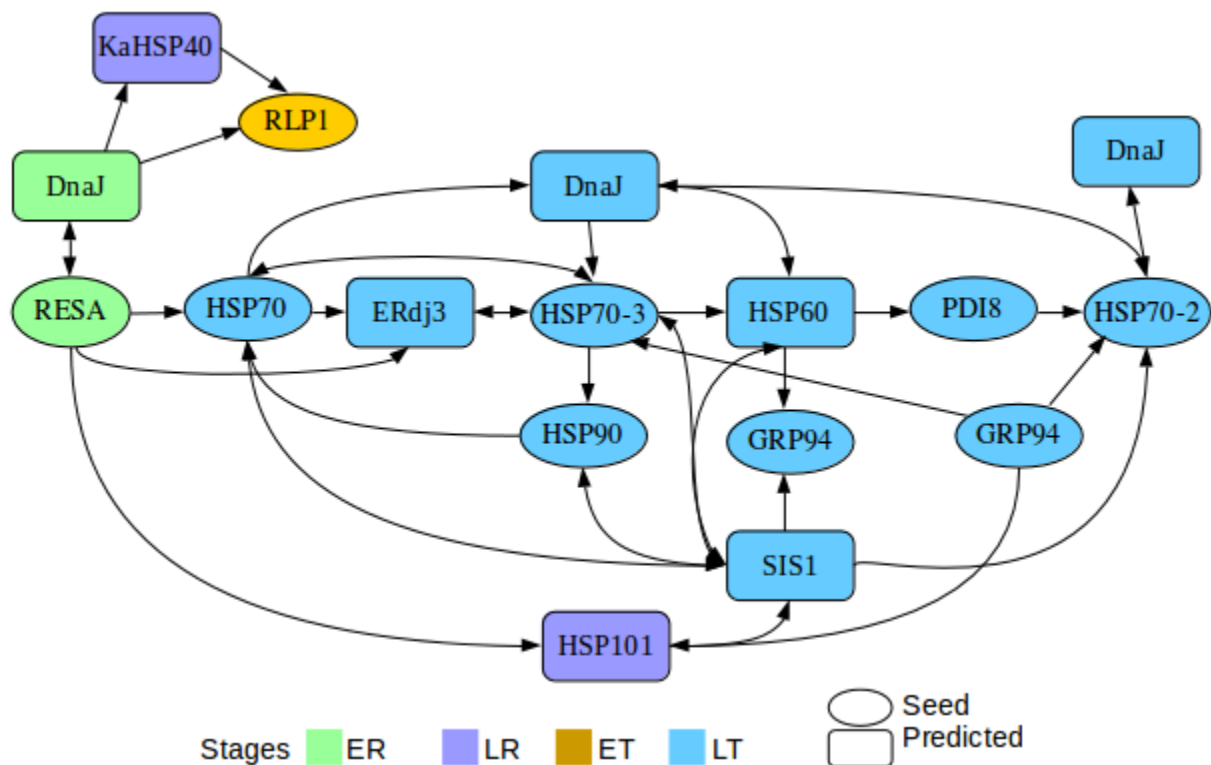


Figure S1: PPI subnetwork with peak-gene expression of heat shock proteins involved in cellular response to heat stress and their neighbors. The stages have been color coded as: ER (green), LR (violet), ET (orange), LT (blue). Though the proteins have been shown to belong to a single stage, it must be noted that, these proteins are also expressed in other stages of the IDC. The abbreviations are: HSP (Heat shock protein), RESA (Ring-infected erythrocyte surface antigen) and PDI (Protein disulfide isomerase). The RWR seed proteins have been shown in oval nodes while the RWR predicted proteins have been shown in rectangular boxes.

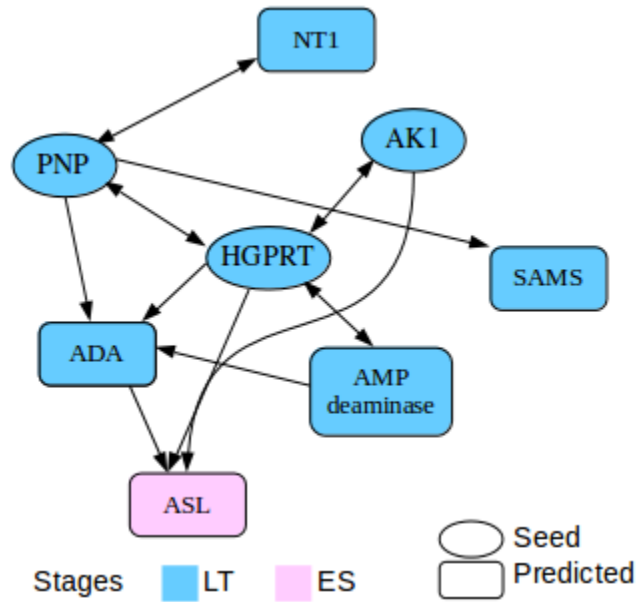


Figure S2: Subnetwork of proteins involved in purine salvage. Almost all these genes have peak-expression at LT stage, except ASL, which has peak gene-expression at LS stage. Seed proteins are in oval boxes, whereas RWR-predicted proteins are shown in rectangular boxes.

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