Supporting Information

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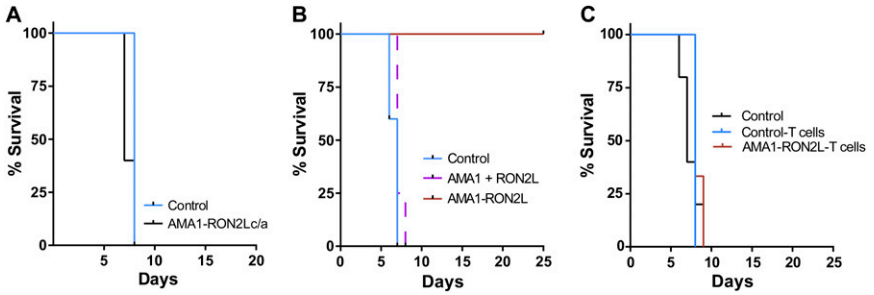

Fig. S1. (*A*) Kaplan–Meier curve of the overall survival of animals in Fig. 1*F*. (*B*) Kaplan–Meier curve of the overall survival of animals in Fig. 1*G*. (*C*) T-cell transfer does not protect against *Py*YM challenge. Kaplan–Meier curve of the overall survival of animals after passive transfer of 2×10^6 T cells from mice immunized with PBS-adjuvant (blue) or mice immunized with *Py*AMA1-RON2L complex (red) on days −1, 0, and +1. Mice that received no cells were used as infection controls (black). Five mice per group were used and were challenged with 10^5 *Py*YM parasites i.v. on day 0.

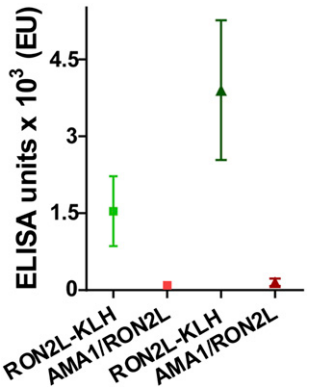

Fig. S2. Anti-PfRON2L antibody titers induced by *Pf*RON2L-KLH and *Pf*AMA1-RON2L complex in rats. ELISA units represent the RON2L-specific antibody titer in either purified IgG (2 mg/mL) or serum from four immunized rats used in Fig. 2*A*. Error bars indicate mean ± SEM.

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          Loop Ib       Loop Ic          Loop Id          Loop Ie          Loop If
        166      177   183   191   195            211   224        235  262          276
         |        |    |     |     |              |     |          |    |            |
D10  ..LTPVATGNQYLK...FPPTEPLMS...LDEMRHFYKDNKYVKNL...MIPDNDKNSNYKY..YCNKDESKRNSMFCF...
3D7  ..LTPVATGNQYLK...FPPTEPLMS...LDEMRHFYKDNKYVKNL...MIPDNDKNSNYKY..YCNKDESKRNSMFCF...
DD2  ..LTPVATGNQYLK...FPPTKPLMS...LDDMRLLYKDNEDVKNL...MNPDNDKNSNYKY..YCNKDESKRNSMFCF...
HP47..LTPVATENQDLK...FPPTEPLMS...LDDMRRFYKDNEYVKNL...MNPDNDKNSNYKY..YCNKDESKRNSMFCF...
HB3  ..LTPVATENQDLK...FPPTEPLIS...LDQMRHLYKDNEYVKNL...MNPDNDKNSNYKY..YCNKDESKRNSMFCF...
CAMP..LKPVATGNQDLK...FPPTEPLIS...LNGMRDFYKNNEYVKNL...MNPDKDENSNYKY..YCNKDESKRNSMFCF...
FVO  ..LKPVATGNQDLK...FPPTNPLIS...LNGMRDFYKNNEYVKNL...MNPDNDKNSNYKY..YCNKDQSKRNSMFCF...
7G8  ..LKPVATGNQDLK...FPPTNPLIS...LDHMRDFYKNNEYVKNL...MNPDNDKNSNYKY..YCNKDESKRNSMFCF...
HP22..LKPVATGNQDLK...FPPTEPLIS...LDDMRDFYKNNEYVKNL...MNPDNDKNSNYKY..YCNKDQSKRNSMFCF...
M24  ..LTPVATENQDLK...FPPTKPLMS...LDQMRDFYKNNEYVKNL...MNPDNDENSNYKY..YCNKDQSKRNSMFCF...
       *.**** ** **   ****:**:*   *: ** :**:*: ***    * **:*:******  *****:*********
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Fig. S3. Sequence alignment showing polymorphisms in the individual domain I loops surrounding the hydrophobic groove across multiple *Plasmodium falciparum* parasite strains.

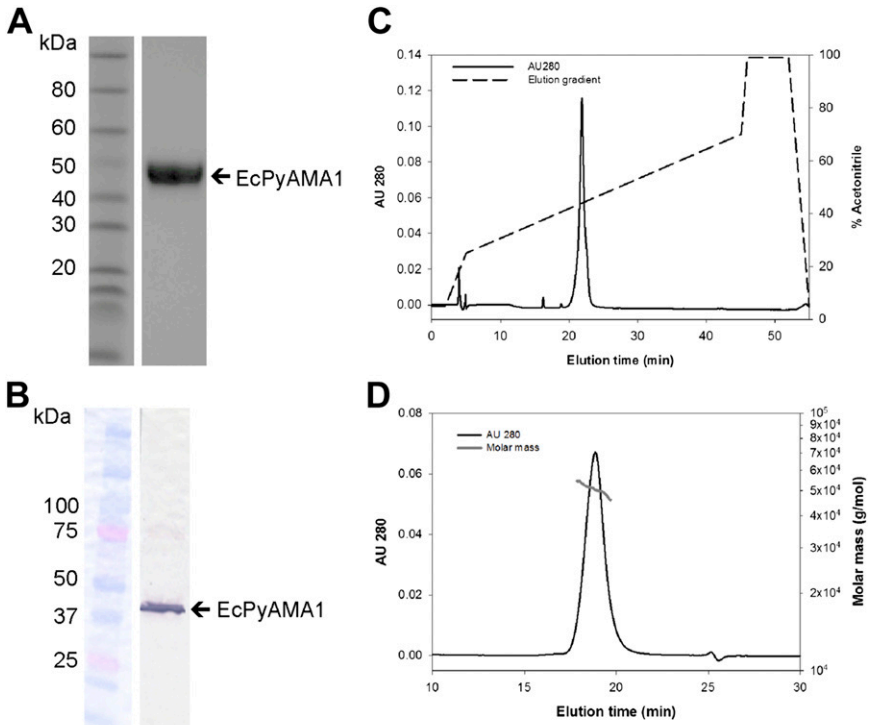

Fig. S4. Biochemical and biophysical characterization of recombinant Ec*Py*AMA1. (*A* and *B*) Analysis of purified recombinant Ec*Py*AMA1 by Coomassie blue-stained SDS/PAGE gel (*A*) and Western blot with a *Py*AMA1-specific mAb 45B1 under nonreduced conditions (*B*). Molecular mass markers are shown alongside. (*C*) Reversed-phase HPLC analysis showing a single peak along with the acetonitrile gradient elution. (*D*) Analytical size-exclusion chromatography showing a single monomeric peak.

PyRON2L: KLH-cDITQHATDIGMGPSTSCYTSLLPPPKSICIQQTVKTVLTNSTLASMK-NH2

PyRON2L: Biotin-Ahx-DITQHATDIGMGPSTSCYTSLLPPPKSICIQQTVKTVLTNSTLASMK-NH2

Pf3D7RON2L: KLH-cDITQQAKDIGAGPVASCFTTRMSPPQQICLNSVVNTALSTSTQSAMK-NH2

Pf3D7RON2L: Biotin-Ahx-DITQQAKDIGAGPVASCFTTRMSPPQQICLNSVVNTALSTSTQSAMK-NH2

Pf3D7_DIa: Biotin-Ahx-LGEDAEVAGTQYRLPS-NH2

Pf3D7_DIb: Biotin-Ahx-ENSNTTFLTPVATGNQYLKDGGFA-NH2

Pf3D7_DId: Biotin-Ahx-TLDEMRHFYKDNKYVK-NH2

Pf3D7_DIe: Biotin-Ahx-GNMIPDNDKNSNYK-NH2

Pf3D7_DIf: Biotin-Ahx-RYCNKDESKRNSMFCFR-NH2

Pf3D7_DII: Biotin-Ahx-SDQPKQYEQHLTDYEKIKEGFKNKNASMIKSAFLPTGAFKADRYKSH-NH2

Pf3D7_DId+e: Biotin-Ahx-SPMTLDEMRHFYKDNKYVKNLDELTLCSRHAGNMIPDNDKNSNYKYPAVYDDKDKKCH-NH2

Pf3D7_DIb+c+d: Biotin-Ahx-SNTTFLTPVATGNQYLKDGGFAFPPTEPLMSPTLDEMRHFYKDNKYVKNL-NH2

Fig. S5. Peptide sequences corresponding to *Py*RON2L, *Pf* RON2L, and *Pf*AMA1 domain I and domain II loop regions used in this study. Disulfide bridged cysteine residues in the peptides are underlined. All peptides were amidated (NH2) at the C terminus.