

**Original Article (Supplementary Information)**

**Clinicopathological Analysis and Multipronged Quantitative Proteomics  
Reveal Oxidative Stress and Cytoskeletal Proteins as Possible Markers for  
Severe Vivax Malaria**

Sandipan Ray<sup>1†\*</sup>, Sandip K.Patel<sup>1†</sup>, Apoorva Venkatesh<sup>1</sup>, Amruta Bhave<sup>1</sup>, Vipin Kumar<sup>1</sup>, Vaidhvi Singh<sup>1</sup>, Gangadhar Chatterjee<sup>3</sup>, Veenita G. Shah<sup>1,9</sup>, Sarthak Sharma<sup>1</sup>, Durairaj Renu<sup>10</sup>, Nazeefa Nafis<sup>1</sup>, Prajakta Gandhe<sup>2</sup>, Nithya Gogtay<sup>2</sup>, Urmila Thatte<sup>2</sup>, Kunal Sehgal<sup>4</sup>, Sumit Verma<sup>5</sup>, Avik Karak<sup>5</sup>, Dibbendhu Khanra<sup>5</sup>, Arunansu Talukdar<sup>5</sup>, Sanjay K. Kochhar<sup>6</sup>, Vijeth S.B<sup>6</sup>, Dhanpat K. Kochhar<sup>6,11</sup>, Dharmendra Rojh<sup>6</sup>, Santosh G. Varma<sup>3</sup>, Mayuri N. Gandhi<sup>7</sup>, Rapole Srikanth<sup>8</sup>, Swati Patankar<sup>1</sup> and Sanjeeva Srivastava<sup>1‡</sup>

<sup>1</sup> Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India

<sup>2</sup> Departments of Clinical Pharmacology, Seth GS Medical College & KEM Hospital, Parel, Mumbai 400012, India

<sup>3</sup> Dept of Biochemistry, Grant Govt Medical College and Sir JJ Group of Hospitals, Byculla, Mumbai 400008, India

<sup>4</sup> PD Hinduja National Hospital & Medical Research Centre, Veer Savarkar Marg, Mahim, Mumbai 400016, India

<sup>5</sup> Medicine Department, Medical College Hospital Kolkata, 88, College Street, Kolkata 700073, India

<sup>6</sup> Department of Medicine, Malaria Research Center, S.P. Medical College, Bikaner 334003, India

<sup>7</sup> Centre for Research in Nanotechnology & Science, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India

<sup>8</sup> Proteomics Laboratory, National Centre for Cell Science, Ganeshkhind, Pune 411007, India  
<sup>9</sup> Wipro GE Healthcare, Mumbai, India

<sup>10</sup> Strand Life Sciences Pvt. Ltd., Hebbal, Bangalore 560024, India

<sup>11</sup> Department of Medicine, RUHS College of Medical Sciences, Jaipur, Rajasthan 302033

† These authors contributed equally to this work.

‡ Correspondence: Dr. Sanjeeva Srivastava, E-mail: sanjeeva@iitb.ac.in  
Phone: +91-22-2576-7779, Fax: +91-22-2572-3480

\* Present address: Department of Clinical Biochemistry, Metabolic Research Laboratories, Wellcome Trust-Medical Research Council Institute of Metabolic Science, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 0QQ, United Kingdom

## A. Supplementary Tables

**Table S1.** Demographics and clinical details of severe and non-severe vivax malaria, dengue fever and leptospirosis patients.

**Table S2.** Details of statistically significant ( $p < 0.05$ ) differentially abundant protein spots in severe vivax malaria compared to healthy controls (A) and non-severe vivax malaria (B) visualized in 2D-DIGE.

**Table S3.** Complete list of MALDI-TOF/TOF identified differentially abundant proteins in vivax malaria detected in 2D-DIGE analysis.

**Table S4.** Complete list of differentially abundant proteins in non-severe (A) and severe (B) vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-TOF mass spectrometer.

**Table S5.** Complete list of differentially abundant proteins in non-severe (A) and severe (B) vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-Exactive mass spectrometer.

**Table S6.** Details of the pathways and networks associated with the differentially abundant serum proteins identified in severe and non-severe vivax malaria defined by IPA, PANTHER and DAVID analysis.

**Table S7.** ELISA-based measurement of serum proteins in healthy community controls, severe and non-severe vivax malaria, dengue fever and leptospirosis patients.

**Table S8.** Statistical summary of ROC curve analysis for evaluating performance of different serum proteins for prediction of non-severe and severe vivax malaria

**Table S9.** Calibration-free concentration analysis (CFCA) for serum amyloid A (SAA) in serum samples of healthy community controls, non-severe and severe vivax malaria, and dengue fever patients.

**Table S10.** Measurement of superoxide dismutase (SOD) activity in healthy community controls, non-severe and severe vivax malaria patients.

**Table S11.** Measurement of serum levels of thiobarbituric acid reactive substances (TBARS) in healthy community controls, non-severe and severe vivax malaria patients.

**Table S2.A:** Age and gender of patients with non-severe and severe malaria, dengue fever and leptospirosis

Age	HC	NSVM	SVM	DF	LEP
<b>18-20</b>	38 (26%)	22 (13.2%)	7 (20.5%)	4 (12.9%)	2 (15.3%)
<b>21-40</b>	67 (45.8%)	98 (59%)	16 (47%)	20 (64.5%)	7 (53.8%)
<b>41-60</b>	39 (26.7%)	45 (27.1%)	10 (29.4%)	7 (22.5%)	3 (23%)
<b>&gt;60</b>	2 (1.3%)	1 (0.6%)	1 (2.9%)	0	1 (7.6%)
<b>Total</b>	<b>146</b>	<b>166</b>	<b>34</b>	<b>31</b>	<b>13</b>

Gender	HC	NSVM	SVM	DF	LEP
<b>Male</b>	77 (52.7%)	140 (84.3%)	24 (70.5%)	19 (61.2%)	10 (76.9%)
<b>Female</b>	69 (47.2%)	26 (15.6%)	10 (29.4%)	12 (38.7%)	3 (23%)
<b>Total</b>	<b>146</b>	<b>166</b>	<b>34</b>	<b>31</b>	<b>13</b>

**Table S1.B:** Laboratory parameters: vivax malaria

Sample	Analysis	Hemoglobin (g/dL)	Platelets (Counts x 10 <sup>9</sup> /L)	Creatinine (mg/dL)	Total bilirubin (mg/dL)	AST (UI/L)	ALT (UI/L)	ALP (UI/L)
<b>HC (n = 146)</b>	Mean	12.9±1.35	297.0±94.3	0.96±0.58	0.80±0.37	29.5±11.5	31.7±12.3	96.0±30.4
<b>NSVM (n = 166)</b>	Mean	12.2±1.79	159.9±92.0	1.03±0.21	1.16±0.62	46.0±53.8	38.5±24.9	92.2±33.8
	p-value	1.56E-06	6.71E-27	1.56E-05	5.89E-08	2.79E-11	0.101119	0.046275
<b>SVM (n = 34)</b>	Mean	10.0±3.49	89.0±90.4	1.52±1.31	2.96±2.45	61.3±40.2	55.9±35.4	169.3±96.3
	p-value	1.20E-08	9.80E-15	1.70E-02	3.10E-13	2.30E-07	1.10E-05	5.70E-08
<b>DF (n = 31)</b>	Mean	11.3±2.61	112.3±65.9	1.12±1.26	1.59±1.42	138.0±143.8	122.5±117.4	137.8±58.8
	p-value	2.90E-04	2.50E-15	1.40E-01	5.50E-04	1.30E-13	4.20E-14	1.00E-04
<b>LEP (n = #)</b>	Mean	11.2±2.57	98.1±77.1	3.36±3.05	4.48±7.34	71.1±45.6	49.3±24.1	81.1±21.1
	p-value	9.30E-04	1.22E-07	0.330522	1.88E-04	1.16E-04	0.041	0.078

#Variable

**Table S1.C:** Organ involvement in severe vivax malaria

Organ system	SVM (n = 34)
Thrombocytopenia	23 (67.6%)
Hepatic	13 (38.2%)
Renal	6 (17.6%)
Cerebral	1 (2.9%)
Lungs	0

**Table S2.A:** Details of all statistically significant ( $p < 0.05$ ) up-regulated (A) and down-regulated (B) proteins spots in severe vivax malaria (compared to healthy controls) visualized in 2D-DIGE

A. Up-regulated spots				
SI. No.	Master No.	Appearance	p-value (t-test)	Av. Ratio
1	685	9 (9)	2.10E-06	4.58
2	721	9 (9)	0.0059	3.5
3	826	9 (9)	0.00013	3.37
4	849	9 (9)	0.007	3
5	833	9 (9)	0.0031	2.99
6	525	9 (9)	0.028	2.86
7	739	9 (9)	0.008	2.84
8	846	9 (9)	0.042	2.81
9	1083	9 (9)	0.047	2.78
10	714	9 (9)	0.0089	2.67
11	529	9 (9)	0.0091	2.54
12	788	9 (9)	0.00089	2.44
13	1101	9 (9)	0.021	2.33
14	461	9 (9)	0.0023	2.28
15	1085	9 (9)	0.0035	2.26
16	499	9 (9)	0.012	2.26
17	1086	9 (9)	0.0054	2.23
18	805	9 (9)	0.031	2.2
19	680	9 (9)	0.0058	2.17
20	839	9 (9)	0.0017	2.16
21	485	9 (9)	0.00091	2.14
22	806	9 (9)	0.043	2.14
23	834	9 (9)	0.0095	2.13
24	823	9 (9)	0.00019	2.12
25	150	9 (9)	0.0019	2.11
26	795	9 (9)	0.0071	2.09
27	875	9 (9)	0.016	2.08
28	147	9 (9)	0.0057	2.03
29	173	9 (9)	0.0045	2.02
30	814	9 (9)	0.0066	2.02
31	929	9 (9)	0.009	2.01
32	465	9 (9)	0.043	2
33	639	9 (9)	0.003	1.97
34	149	9 (9)	0.0094	1.95
35	845	9 (9)	0.00052	1.93
36	306	9 (9)	0.0025	1.93
37	1092	9 (9)	0.016	1.92
38	304	9 (9)	0.0032	1.88
39	1113	9 (9)	0.0023	1.84
40	720	9 (9)	0.00029	1.83

41	1117	9 (9)	0.0022	1.83
42	462	9 (9)	0.019	1.83
43	1106	9 (9)	0.022	1.83
44	154	9 (9)	0.037	1.82
45	837	9 (9)	0.0017	1.81
46	297	9 (9)	0.00019	1.79
47	153	9 (9)	0.02	1.79
48	641	9 (9)	0.0068	1.75
49	740	9 (9)	0.0015	1.74
50	867	9 (9)	0.00012	1.73
51	895	9 (9)	0.036	1.72
52	148	9 (9)	0.0052	1.68
53	151	9 (9)	0.0032	1.66
54	864	9 (9)	0.022	1.65
55	468	9 (9)	0.0031	1.61
56	1097	9 (9)	0.0097	1.61
57	429	9 (9)	0.0043	1.6
58	484	9 (9)	0.0098	1.6
59	865	9 (9)	0.001	1.58
60	724	9 (9)	0.013	1.58
61	1093	9 (9)	0.048	1.58
62	686	9 (9)	0.021	1.57
63	223	9 (9)	0.034	1.57
64	879	9 (9)	0.0063	1.56
65	1098	9 (9)	0.023	1.56
66	820	9 (9)	0.032	1.55
67	470	9 (9)	0.0023	1.54
68	175	9 (9)	0.021	1.54
69	810	9 (9)	0.041	1.54
70	852	9 (9)	0.048	1.54
71	715	9 (9)	0.0016	1.53
72	535	9 (9)	0.018	1.53
73	825	9 (9)	0.0016	1.52
74	757	9 (9)	0.019	1.52
75	146	9 (9)	0.0031	1.51

B. Down-regulated spots				
SI. No.	Master No.	Appearance	p-value (t-test)	Av. Ratio
1	744	9 (9)	0.01	-1.52
2	705	9 (9)	0.0085	-1.56
3	64	9 (9)	0.01	-1.56
4	682	9 (9)	0.03	-1.6
5	257	9 (9)	0.0027	-1.61
6	635	9 (9)	0.00	-1.61

7	970	6 (9)	0.02	-1.61
8	263	9 (9)	0.0036	-1.62
9	492	9 (9)	0.02	-1.66
10	1090	9 (9)	2.80E-05	-1.68
11	579	9 (9)	0.03	-1.72
12	368	9 (9)	0.02	-1.73
13	1001	9 (9)	0.0004	-1.75
14	687	9 (9)	0.03	-1.81
15	92	9 (9)	0.0038	-1.82
16	730	9 (9)	0.0031	-1.83
17	1111	9 (9)	0.0023	-1.84
18	662	9 (9)	0.0037	-1.86
19	133	9 (9)	0.00065	-1.87
20	416	9 (9)	0.0038	-1.89
21	412	9 (9)	0.00019	-2.1
22	697	9 (9)	0.0022	-2.1
23	603	9 (9)	0.01	-2.28
24	501	9 (9)	0.0019	-2.29
25	1084	9 (9)	0.01	-2.41
26	415	9 (9)	1.10E-05	-2.54
27	626	9 (9)	0.02	-2.6
28	1112	9 (9)	0.0084	-2.61
29	976	9 (9)	0.04	-2.95
30	683	9 (9)	0.0079	-3.03
31	975	9 (9)	0.0012	-3.1
32	980	9 (9)	0.0017	-3.31
33	667	9 (9)	0.00066	-3.41
34	624	9 (9)	0.0085	-3.64
35	1035	9 (9)	0.01	-3.69
36	1076	9 (9)	0.02	-3.8
37	1079	9 (9)	0.00058	-3.94
38	1051	9 (9)	0.0029	-4.19
39	668	9 (9)	5.30E-05	-4.27
40	700	9 (9)	0.00	-4.28
41	1081	9 (9)	0.0032	-4.66
42	1037	9 (9)	0.0021	-4.83
43	688	9 (9)	0.00	-5.36
44	1088	9 (9)	0.00081	-5.7
45	1080	9 (9)	0.01	-5.89
46	675	9 (9)	0.00036	-6.02
47	1087	9 (9)	0.0027	-6.17
48	445	9 (9)	0.00011	-6.18
49	1089	9 (9)	0.00062	-6.29
50	643	9 (9)	0.0072	-6.47
51	1052	9 (9)	0.00	-6.56

52	636	9 (9)	0.0093	-7.05
53	1077	9 (9)	0.0042	-9.16
54	1078	9 (9)	0.0024	-9.25
55	979	9 (9)	0.0035	-11.04
56	1038	9 (9)	4.50E-07	-18.6

**Table S2.B:** Details of all statistically significant ( $p < 0.05$ ) up-regulated (A) and down-regulated (B) proteins spots in severe vivax malaria (compared to non-severe vivax malaria) visualized in 2D-DIGE.

A. Up -Regulated spots				
SI. No.	Master No.	Appearance	p-value (t-test)	Av. Ratio
1	857	9 (9)	0.0033	2.47
2	1046	9 (9)	0.024	2.3
3	89	9 (9)	0.025	2.27
4	562	9 (9)	0.011	2.25
5	873	9 (9)	0.026	2.05
6	532	9 (9)	1.60E-06	1.98
7	609	9 (9)	0.00031	1.97
8	53	9 (9)	0.0044	1.97
9	894	9 (9)	0.033	1.94
10	169	9 (9)	0.016	1.92
11	725	9 (9)	0.00021	1.87
12	20	9 (9)	0.03	1.77
13	973	9 (9)	0.026	1.76
14	968	9 (9)	0.032	1.75
15	604	9 (9)	0.0018	1.67
16	804	9 (9)	0.012	1.67
17	792	9 (9)	0.017	1.64
18	821	9 (9)	0.046	1.62
19	849	9 (9)	0.032	1.6
20	42	9 (9)	0.027	1.57

B. Down Regulated spots				
SI. No.	Master No.	Appearance	p-value (t-test)	Av. Ratio
1	82	9 (9)	0.018	-1.51
2	316	9 (9)	0.032	-1.51
3	329	9 (9)	0.012	-1.53
4	88	9 (9)	0.029	-1.64
5	318	9 (9)	0.049	-1.66
6	94	9 (9)	0.038	-1.72

**Table S3.** Master tables for MALDI-TOF/TOF identified differentially abundant proteins in severe vivax malaria (compared to healthy controls) 2D-DIGE experiment  
 [Analysis Type: Combined (MS+MS/MS); Database: SwissProt; Taxonomy: *Homo sapiens*]

Sl. No.	Gel ID	Fold change	Protein name	Uniprot ID	Mol. wt.	Protein score	Total ion score	Matched peptides
1	826	3.37	Serum amyloid P component precursor	P02743	25.37	179	144	7
2	1101	2.33	Alpha-1-antitrypsin precursor (alpha-1 protease inhibitor)	P01009	46.7	152	84	14
3	680	2.17	Clusterin precursor (complement associated protein SP-40)	P10909	52.46	210	201	7
4	485	2.14	Serum amyloid A	P02735	13.52	212	162	7
5	823	2.12	DNA2-like helicase	-	122.04	58	18	22
6	720	1.83	Clusterin	P10909	53.03	86	74	9
7	1098	1.56	Ig alpha-1 chain C region	P01876	37.63	491	432	14
8	715	1.53	Complement C3 precursor	P01024	187.04	57	38	18
9	535	1.53	Alpha-1-antitrypsin precursor (alpha-1 protease inhibitor)	P01009	46.7	101	47	12
10	757	1.52	AMBP protein precursor [contains:Alpha-1- microglobulin] (protein HC)	P02760	38.97	212	163	14
11	1090	-1.68	Leucine-rich alpha-2- glycoprotein precursor (LRG)	P02750	38.15	675	621	11
12	368	-1.73	Alpha-1B-glycoprotein	P04217	54.78	220	188	15
13	1084	-2.41	Apolipoprotein A-1 precursor (Apo-AI)	P02647	30.75	934	719	24
14	415	-2.54	Serum Albumin	P0DJI8	69.32	340	277	28
15	1081	-4.66	Haptoglobin precursor	P00738	45.17	248	198	12
16	688	-5.36	Haptoglobin	P00738	45.86	154	133	11
17	1088	-5.7	Haptoglobin precursor	P00738	45.17	239	192	11
18	636	-7.05	Serum albumin	P0DJI8	69.3	674	619	23
19	1077	-9.16	Haptoglobin	P00738	45.86	357	326	13
20	1087	-6.17	Haptoglobin	P00738	45.17	713	649	14
21	1089	-6.29	Haptoglobin precursor	P00738	45.17	217	150	13
22	1078	-9.25	Haptoglobin	P00738	45.86	118	98	10

**Table S4.A:** Differentially abundant proteins ( $p < 0.05$ ) in non-severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-TOF mass spectrometer

SL No.	UniProt ID	Protein names	Gene names	Log 2 NSVM 1	Log 2 NSVM 2	Log 2 NSVM 3	Log2 HC1	Log2 HC2	Log2 HC3	Ratio NSVM/ HC	-Log Student's t-test p-value	Student's t-test p-value	Unique peptides
1	P0DJ19	Serum amyloid A-2 protein	SAA2	-3.57	-3.58	-3.24	-5.86	-5.20	-4.77	3.38	1.38	0.04143	3
2	P0DJ18	Serum amyloid A-1 protein	SAA1	-0.18	-0.06	-0.17	-1.32	-1.33	-1.32	2.28	5.22	0.00001	5
3	O60813	PRAME family member 11	PRAMEF11	-2.51	-2.71	-2.67	-3.39	-3.42	-4.39	2.05	1.53	0.02954	1
4	P02741	C-reactive protein	CRP	-3.58	-3.29	-3.75	-4.45	-4.79	-4.36	1.99	2.22	0.00606	12
5	P02649	Apolipoprotein E	APOE	-4.38	-4.16	-4.51	-5.14	-5.18	-5.61	1.94	2.21	0.00619	10
6	Q9BRQ5	Protein orai-3	ORAI3	-1.03	-1.38	-1.32	-2.07	-1.75	-2.47	1.78	1.66	0.02211	1
7	P27694	Replication protein A 70 kDa DNA-binding subunit	RPA1	-2.51	-1.96	-2.12	-2.83	-2.73	-3.60	1.77	1.28	0.05208	4
8	P00450	Ceruloplasmin	CP	-0.90	-0.63	-0.93	-1.33	-1.61	-1.92	1.72	1.83	0.01490	25
9	Q5JTH9	RRP12-like protein	RRP12	-1.14	-1.39	-1.21	-2.25	-1.59	-2.23	1.67	1.55	0.02848	2
10	P68871	Hemoglobin subunit beta (Beta-globin)	HBB	-1.48	-1.46	-1.30	-1.87	-1.87	-2.46	1.55	1.50	0.03175	4
11	P10909	Clusterin	CLU	-2.39	-2.81	-2.80	-3.23	-3.14	-3.34	1.50	1.72	0.01908	11
12	P02042	Hemoglobin subunit delta (Delta-globin)	HBD	3.82	3.65	3.70	3.27	3.34	2.78	1.49	1.49	0.03243	10
13	P01011	Alpha-1-antichymotrypsin (ACT)	SERPINA3	1.63	1.66	1.70	1.13	1.21	0.91	1.49	2.46	0.00345	24
14	P01009	Alpha-1-antitrypsin	SERPINA1	-1.22	-1.13	-1.66	-1.96	-1.93	-1.78	1.48	1.50	0.03199	36
15	P00747	Plasminogen	PLG	-3.35	-3.19	-3.07	-3.71	-3.99	-3.53	1.44	1.58	0.02616	17
16	P01861	Ig gamma-4 chain C region	IGHG4	1.38	1.12	1.17	0.88	0.78	0.44	1.43	1.54	0.02870	7
17	Q9UFW8	CGG triplet repeat-binding protein 1	CGGBP1	0.22	0.05	-0.07	-0.21	-0.46	-0.63	1.41	1.54	0.02868	3
18	P02790	Hemopexin	HPX	2.62	2.92	2.72	2.28	2.28	2.26	1.40	2.25	0.00563	16
19	P01877	Ig alpha-2 chain C region	IGHA2	2.30	2.30	2.36	1.99	1.97	1.53	1.39	1.49	0.03250	19

20	Q86UW 7	Calcium-dependent secretion activator 2	CADPS2	-1.06	-1.08	-0.94	-1.24	-1.56	-1.66	1.36	1.59	0.02591	1
21	P00734	Prothrombin (EC 3.4.21.5)	F2	0.56	0.55	0.68	0.25	0.33	-0.08	1.34	1.51	0.03087	15
22	P54277	PMS1 protein homolog 1	PMS1	1.23	1.13	1.15	0.85	0.90	0.51	1.32	1.52	0.03011	2
23	P02750	Leucine-rich alpha-2-glycoprotein	LRG	-0.09	0.06	0.07	-0.46	-0.17	-0.44	1.29	1.59	0.02550	11
24	P04004	Vitronectin	VTN	-0.08	0.03	-0.08	-0.41	-0.22	-0.39	1.23	1.85	0.01425	10
25	P02743	Serum amyloid P-component	APCS	-1.95	-1.90	-2.01	-2.13	-2.18	-2.39	1.21	1.50	0.03156	6
26	P25311	Zinc-alpha-2-glycoprotein	AZGP1	0.79	0.68	0.74	0.50	0.43	0.50	1.20	2.58	0.00262	11
27	P00441	Superoxide dismutase [Cu-Zn]	SOD1	0.24	0.06	0.03	-0.06	-0.07	-0.25	1.18	1.32	0.05791	18
28	Q14204	Cytoplasmic dynein 1 heavy chain 1	DYNC1H1	-1.35	-1.30	-1.42	-1.14	-0.97	-0.73	0.75	1.48	0.03274	2
29	P05156	Complement factor I	CFI IF	-0.866	-0.458	-0.608	-0.238	-0.338	0.094	0.714	1.29	0.05102	9
30	P02671	Fibrinogen alpha chain	FGA	-3.027	-3.214	-3.454	-2.707	-2.611	-2.262	0.612	1.74	0.01834	21
31	P00739	Haptoglobin-related protein	HPR	0.906	0.851	0.857	1.627	1.297	1.858	0.599	1.94	0.01155	28
32	P02647	Apolipoprotein A-I	APOA1	0.5035	0.593	0.4764	0.8125	1.240	1.696	0.587	1.32	0.04808	18
33	P06727	Apolipoprotein A-IV	APOA4	1.317	1.446	1.490	1.900	2.009	2.588	0.583	1.57	0.02713	16
34	P02768	Serum albumin	ALB	2.751	3.085	2.860	3.473	4.120	4.153	0.486	1.86	0.01371	28
35	P00738	Haptoglobin (Zonulin)	HP	0.081	0.316	0.281	1.482	1.522	1.346	0.429	3.76	0.00017	18

Values are log2 transformed, and normalization was performed by “subtract (mean)” and Z-score normalization

**Table S4.B:** Differentially abundant proteins ( $p < 0.05$ ) in severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-TOF mass spectrometer

SL No.	UniProt ID	Protein names	Gene names	Log 2 SVM1	Log 2 SVM2	Log 2 SVM3	Log2 HC1	Log2 HC2	Log2 HC3	Ratio SVM/HC	-Log Student's t-test p-value	Student's t-test p-value	Unique peptides
1	P0DJI8	Serum amyloid A-1	SAA1	-0.98	-1.32	-1.40	-3.57	-3.50	-3.33	4.73	3.95	0.000112	5
2	A4D1E1	Zinc finger protein	ZNF804B	0.37	-0.05	-0.32	-1.42	-1.39	-1.46	2.75	2.67	0.002155	1
3	P02649	Apolipoprotein E	APOE	1.05	1.20	1.02	-0.15	-0.54	-0.27	2.65	3.44	0.000362	10
4	P02741	C-reactive protein	CRP	2.03	2.02	1.91	0.74	0.85	0.70	2.33	4.48	0.000033	12
5	Q8WZ42	Titin	TTN	0.15	-0.31	-0.41	-1.10	-1.29	-1.45	2.15	2.25	0.005678	12
6	P20929	Nebulin	NEB	-2.97	-2.86	-3.03	-3.75	-4.09	-4.09	2.02	2.95	0.001127	3
7	P00450	Ceruloplasmin	CP	0.24	-0.76	-0.59	-1.23	-1.30	-1.30	1.97	1.37	0.042461	25
8	Q9H6E5	PIP5K1A-regulated poly(A) polymerase	TUT1	-1.79	-1.45	-1.50	-2.47	-2.44	-2.36	1.81	2.82	0.001509	1
9	P01011	Alpha-1-antichymotrypsin	SERPINA3	2.01	1.68	1.49	1.04	0.85	0.87	1.76	2.08	0.008273	24
10	Q12766	HMG domain-containing protein 3	HMGXB3	-1.84	-1.65	-1.77	-2.12	-2.73	-2.74	1.68	1.66	0.022004	1
11	P01861	Ig gamma-4 chain C region	IGHG4	0.53	0.80	0.83	0.17	-0.05	0.05	1.59	2.34	0.004589	3
12	P02790	Hemopexin (Beta-1B-glycoprotein)	HPX	3.40	3.17	3.10	2.67	2.57	2.56	1.55	2.51	0.003055	16
13	P01877	Ig alpha-2 chain C region	IGHA2	2.98	2.66	2.77	2.19	2.06	2.29	1.54	2.21	0.006223	19
14	P02763	Alpha-1-acid glycoprotein 1	ORM1	-1.94	-1.88	-2.27	-2.59	-2.61	-2.73	1.54	2.06	0.008614	8
15	P08571	Monocyte differentiation antigen CD14	CD14	0.08	-0.05	0.00	-0.43	-0.69	-0.69	1.53	2.57	0.002681	2
16	P00441	Superoxide dismutase [Cu-Zn]	SOD1	-0.67	-0.78	-0.83	-1.04	-1.49	-1.62	1.52	1.56	0.027360	1
17	P01009	Alpha-1-antitrypsin	SERPINA1	3.09	2.96	3.04	2.41	2.29	2.57	1.52	2.61	0.002452	36
18	P00747	Plasminogen	PLG	-0.17	0.21	0.04	-0.50	-0.70	-0.41	1.49	1.82	0.014971	17
19	Q5VST9	Obscurin	OBSCN	-2.92	-3.14	-2.89	-3.67	-3.34	-3.66	1.48	1.91	0.012403	3
20	P05155	Plasma protease C1 inhibitor	SERPING1	0.01	-0.16	-0.23	-0.70	-0.76	-0.55	1.46	2.33	0.004632	17
21	P10909	Clusterin	CLU	-2.69	-3.04	-2.72	-3.68	-3.07	-3.37	1.46	1.28	0.051964	11
22	Q92896	Golgi apparatus protein 1	GLG1	0.58	0.69	0.58	0.07	0.02	0.13	1.46	3.47	0.000338	2
23	P02743	Serum amyloid P-component	APCS	-2.29	-2.26	-2.23	-2.44	-3.03	-2.94	1.44	1.38	0.041338	6
24	P02042	Hemoglobin subunit delta (Delta-globin)	HBD	-0.38	-0.45	-0.73	-0.97	-1.12	-0.98	1.42	1.88	0.013041	10
25	P04004	Vitronectin	VTN	1.82	1.50	1.29	0.91	1.11	1.12	1.42	1.36	0.043960	10
26	Q96E29	Transcription termination factor 3, mitochondrial	MTERF3	0.22	0.27	-0.08	-0.15	-0.51	-0.42	1.41	1.48	0.03319	3

27	Q9H0H0	Integrator complex subunit 2	INTS2	0.95	0.73	1.04	0.42	0.36	0.54	1.39	1.94	0.011452	2
28	P02750	Leucine-rich alpha-2-glycoprotein	LRG	-1.96	-1.75	-2.11	-2.35	-2.42	-2.34	1.36	1.78	0.016412	11
29	Q8N2S1	Latent-transforming growth factor beta-binding protein 4	LTBP4	-1.40	-1.76	-1.64	-1.94	-2.10	-2.05	1.35	1.68	0.021033	1
30	P52746	Zinc finger protein 142	ZNF142	-0.05	-0.15	-0.16	-0.59	-0.61	-0.44	1.34	2.58	0.002657	1
31	P27694	Replication protein A 70 kDa DNA-binding subunit	RPA1	-1.42	-1.67	-1.63	-1.90	-2.03	-1.99	1.32	2.04	0.009061	4
32	P68871	Hemoglobin subunit beta (Beta-globin)	HBB	-0.85	-0.90	-0.74	-1.17	-1.32	-1.12	1.30	2.10	0.007894	7
33	P25311	Zinc-alpha-2-glycoprotein	AZGP1	-0.80	-0.85	-0.82	-1.14	-1.30	-1.07	1.27	2.08	0.008353	11
34	P04114	Apolipoprotein B-100	APOB	1.74	1.56	1.69	1.43	1.22	1.34	1.26	1.84	0.014338	111
35	P19823	Inter-alpha-trypsin inhibitor heavy chain H2	ITIH2	-1.03	-0.97	-1.00	-1.22	-1.49	-1.28	1.25	1.74	0.018118	10
36	P05156	Complement factor I	CFI IF	-1.65	-1.68	-1.76	-1.51	-1.51	-1.43	0.86	2.23	0.005849	9
37	P06727	Apolipoprotein A-IV	APOA4	-0.39	-0.22	-0.13	0.17	0.15	0.24	0.74	2.21	0.006174	16
38	P35354	Prostaglandin G/H synthase 2	PTGS2	-2.61	-2.33	-2.28	-2.13	-1.71	-2.02	0.73	1.32	0.047448	1
39	P29622	Kallistatin	SERPINA4	-2.57	-2.37	-2.30	-1.91	-1.99	-1.89	0.72	2.29	0.005160	2
40	P32119	Peroxiredoxin-2	PRDX2	-1.18	-0.63	-1.00	-0.38	-0.36	-0.35	0.68	1.62	0.024121	3
41	Q8WXD5	Gem-associated protein 6	GEMIN6	-0.48	0.07	-0.22	0.21	0.65	0.25	0.67	1.29	0.051348	1
42	Q96AJ1	Clusterin-associated protein 1	CLUAP1	-0.79	-1.00	-0.84	-0.51	0.05	-0.33	0.64	1.60	0.024908	1
43	P02766	Transthyretin	TTR	-1.41	-1.41	-1.27	-0.94	-0.50	-0.65	0.63	2.10	0.007964	8
44	Q9ULX5	RING finger protein 112	RNF112	0.64	0.87	0.80	1.28	1.88	1.41	0.59	1.74	0.018085	1
45	P02768	Serum albumin	ALB	5.13	5.32	5.27	5.95	6.11	6.10	0.57	3.37	0.000424	28
46	Q13601	KRR1 small subunit processome component homolog	KRR1	-1.72	-1.65	-1.31	-0.39	-1.05	-0.75	0.56	1.65	0.022507	1
47	P02647	Apolipoprotein A-I	APOA1	3.12	3.16	3.29	4.13	4.14	4.09	0.53	4.19	0.000065	18
48	Q14BN4	Sarcolemmal membrane-associated protein	SLMAP	-3.81	-3.54	-3.95	-2.88	-2.72	-2.83	0.52	2.74	0.001837	2
49	P02652	Apolipoprotein A-II	APOA2	-4.65	-3.35	-3.71	-2.77	-2.70	-2.67	0.47	1.43	0.037187	6
50	O14921	Regulator of G-protein signaling 13	RGS13	-3.40	-2.70	-2.97	-1.79	-1.50	-1.68	0.39	2.47	0.003373	1
51	P00738	Haptoglobin	HP	0.15	0.77	0.56	1.69	2.12	1.93	0.38	2.53	0.002944	18

Values are log2 transformed, and normalization was performed by “subtract (mean)” and Z-score normalization

**Table S5.A:** Differentially abundant (fold-change  $\geq 1.2$  at 1% FDR) proteins in non-severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-Exactive mass spectrometer

SL. No	Accession	# Unique Peptides	NSVM	Description
1	C8C504	4	2.115	Beta-globin
2	B2R950	6	2.099	cDNA, FLJ94213, highly similar to Homo sapiens pregnancy-zone protein
3	C9J6N2	1	2.088	Uroplakin-1b (Fragment) OS
4	U3PXP0	1	2.004	Alpha globin chain (Fragment) OS
5	P0DJI9	3	1.986	Serum amyloid A-2 protein OS
6	D3DQX7	2	1.968	Serum amyloid A protein OS
7	Q4TZM4	2	1.940	Hemoglobin beta chain (Fragment) OS
8	B2R5G8	2	1.921	Serum amyloid A protein OS
9	P0DJI8	1	1.864	Serum amyloid A-1 protein OS
10	Q4G0R1	1	1.793	PIBF1 protein OS
11	I1VZV6	1	1.747	Hemoglobin alpha 1 OS
12	I3L145	2	1.707	Sex hormone-binding globulin OS
13	P02790	28	1.676	Hemopexin OS
14	Q86YQ1	1	1.637	Hemoglobin alpha-2 (Fragment) OS
15	P00450	5	1.621	Ceruloplasmin OS
16	P01009	28	1.593	Alpha-1-antitrypsin OS
17	P02649	9	1.590	Apolipoprotein E OS
18	P02741	5	1.556	C-reactive protein OS
19	P00747	27	1.543	Plasminogen OS
20	P02743	5	1.539	Serum amyloid P-component OS
21	Q6J1Z9	2	1.532	Hemoglobin alpha 1 (Fragment) OS
22	D6RF35	2	1.527	Vitamin D-binding protein OS
23	P04004	12	1.526	Vitronectin OS
24	B2R9V7	2	1.513	Superoxide dismutase [Cu-Zn] OS
25	P00918	1	1.493	Carbonic anhydrase 2 OS
26	P02042	4	1.483	Hemoglobin subunit delta OS
27	Q7KZ85	1	1.465	Transcription elongation factor SPT6 OS
28	P00915	7	1.435	Carbonic anhydrase 1 OS
29	H0YCJ8	1	1.427	Blood group Rh(CE) polypeptide (Fragment) OS
30	B4DF70	3	1.421	cDNA FLJ60461, highly similar to Peroxiredoxin-2 (EC 1.11.1.15) OS
31	Q3ZCV0	1	1.407	SYNE1 protein (Fragment) OS
32	P02750	1	1.403	Leucine-rich alpha-2-glycoprotein OS
33	Q8IVF6	1	1.386	Ankyrin repeat domain-containing protein 18A OS
34	Q9H3B5	1	1.386	PRO1367 OS
35	H2B4M3	1	1.358	LILRA3 protein OS
36	B4DV14	1	1.344	cDNA FLJ60037, highly similar to Napsin-A (EC 3.4.23.-) OS
37	Q59GU3	1	1.321	Voltage-dependent L-type calcium channel alpha-1C subunit variant (Fragment) OS
38	B7Z570	1	1.321	cDNA FLJ53078, highly similar to Splicing factor, arginine/serine-rich 1 OS
39	S6BGE0	1	1.308	IgG H chain OS
40	P01861	2	1.279	Ig gamma-4 chain C region OS
41	B3KME0	1	1.278	cDNA FLJ10760 fis, clone NT2RP3004618, highly similar to Eukaryotic translation initiation factor 2C 1 OS

42	A2MYC8	2	1.267	V5-2 protein (Fragment) OS
43	Q5SXM1	1	1.267	Zinc finger protein 678 OS
44	O43825	1	1.261	Beta-1,3-galactosyltransferase 2 OS
45	S6BGD6	1	1.253	IgG L chain OS
46	Q5NV92	2	1.252	V5-6 protein (Fragment) OS
47	H0YJC6	1	1.249	Processed lymphoid-restricted membrane protein (Fragment) OS
48	B3KWB5	1	1.245	cDNA FLJ42722 fis, clone BRAMY4000277, highly similar to Alpha-1B-glycoprotein OS
49	P19652	7	1.244	Alpha-1-acid glycoprotein 2 OS
50	A6XND1	1	1.242	Insulin-like growth factor binding protein 3 isoform b OS
51	A2KBC6	1	1.237	Anti-FactorVIII scFv (Fragment) OS
52	Q9NZP8	2	1.236	Complement C1r subcomponent-like protein OS
53	B7Z539	2	1.226	cDNA FLJ56954, highly similar to Inter-alpha-trypsin inhibitor heavy chain H1 OS
54	B2R6W1	1	1.225	cDNA, FLJ93143, highly similar to Homo sapiens complement component 7 (C7), mRNA OS
55	Q8N355	1	1.225	IGL@ protein OS
56	B1ANW7	1	1.220	Nebulin-related-anchoring protein OS
57	Q8TCF0	5	1.218	LBP protein OS
58	D3DPI9	1	1.213	Signal transducer and activator of transcription 4, isoform CRA_a OS
59	H7C0U4	1	1.212	EF-hand domain-containing family member B (Fragment) OS
60	P02655	3	1.211	Apolipoprotein C-II OS
61	P02748	15	1.206	Complement component C9 OS
62	P04053	1	1.205	DNA nucleotidylexotransferase OS
63	Q9UL83	1	1.203	Myosin-reactive immunoglobulin light chain variable region (Fragment) OS
64	P01606	1	1.202	Ig kappa chain V-I region OU OS
65	B1AKG0	1	1.201	Complement factor H-related protein 1 OS
66	P05546	12	0.831	Heparin cofactor 2 OS
67	D6R963	1	0.830	Uncharacterized protein OS
68	Q5SRP5	4	0.828	Apolipoprotein M OS
69	B3KQV6	1	0.827	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform OS
70	E5RFX7	1	0.826	Proline synthase co-transcribed bacterial homolog protein (Fragment) OS
71	K7EQB3	1	0.822	Sia-alpha-2,3-Gal-beta-1,4-GlcNAc-R:alpha 2,8-sialyltransferase (Fragment) OS
72	A2NW98	1	0.821	Rheumatoid factor light chain variable region (Fragment) OS
73	H0YLF3	1	0.820	Beta-2-microglobulin form pI 5.3 (Fragment) OS
74	B4E344	1	0.820	cDNA FLJ54406, highly similar to Complement C4-B OS
75	P10599	1	0.819	Thioredoxin OS
76	A0PJG0	2	0.816	THBS1 protein (Fragment) OS
77	P01833	2	0.814	Polymeric immunoglobulin receptor OS
78	A0M8Q6	3	0.812	Ig lambda-7 chain C region OS
79	Q76B58	1	0.805	BMP/retinoic acid-inducible neural-specific protein 3 OS
80	B7ZLE5	34	0.801	FNI protein OS
81	P01034	2	0.800	Cystatin-C OS
82	Q65ZC9	1	0.799	Single-chain Fv (Fragment) OS
83	Q9HAI6	1	0.793	Uncharacterized protein CXorf21 OS
84	B3KX47	1	0.790	cDNA FLJ44733 fis, clone BRACE3026290, highly similar to Lethal(2) giant larvae protein homolog 2 OS
85	P02776	3	0.789	Platelet factor 4 OS
86	B2RCH7	1	0.788	cDNA, FLJ96082, highly similar to Homo sapiens cervical cancer 1 protooncogene (HCCR1), mRNA OS
87	G3XAD3	1	0.784	Glutamate receptor ionotropic, kainate 2 OS

88	H7C598	1	0.769	Protein DENND6A (Fragment) OS
89	Q13789	1	0.767	Apolipoprotein B (Fragment) OS
90	A4LAA3	1	0.762	Alpha thalassemia/mental retardation syndrome X-linked OS
91	C9J8U1	1	0.758	Cytospin-A (Fragment) OS
92	D3JV41	4	0.758	Thrombocidin-2 antimicrobial variant (Fragment) OS
93	B3KVK6	2	0.749	Complement factor properdin, isoform CRA_c OS
94	B4E335	6	0.747	cDNA FLJ52842, highly similar to Actin, cytoplasmic 1 OS
95	C9JXV0	1	0.738	Tumor suppressor p53-binding protein 1 (Fragment) OS
96	D9IVD5	1	0.736	Nuclear factor interleukin 3 regulated protein OS
97	O95229	1	0.730	ZW10 interactor OS
98	I3L4A6	1	0.705	Mixed lineage kinase domain-like protein (Fragment) OS
99	F8VV32	1	0.701	Lysozyme C OS
100	Q562M3	1	0.696	Actin-like protein (Fragment) OS
101	E9PFZ2	1	0.684	Ceruloplasmin OS
102	Q6GMX0	1	0.675	Uncharacterized protein OS
103	H0YBS8	1	0.662	Homeobox-containing protein 1 (Fragment) OS
104	COJYY2	135	0.647	Apolipoprotein B (Including Ag(X) antigen) OS
105	B7Z284	1	0.643	DNA-directed RNA polymerase OS
106	P35908	14	0.633	Keratin, type II cytoskeletal 2 epidermal OS
107	P00739	6	0.628	Haptoglobin-related protein OS
108	P01023	75	0.619	Alpha-2-macroglobulin OS
109	G3V2B0	1	0.610	MAGUK p55 subfamily member 5 OS
110	O14792	1	0.585	Heparan sulfate glucosamine 3-O-sulfotransferase 1 OS
111	B2R4M6	2	0.573	cDNA, FLJ92148, highly similar to Homo sapiens S100 calcium binding protein A9 (calgranulin B) (S100A9), mRNA OS
112	P06727	22	0.558	Apolipoprotein A-IV OS
113	P02647	20	0.555	Apolipoprotein A-I OS
114	A8K5J7	1	0.541	cDNA FLJ77290, highly similar to Homo sapiens BCL2-associated athanogene 5 (BAG5), mRNA OS
115	P00738	13	0.526	Haptoglobin OS
116	P02533	8	0.500	Keratin, type I cytoskeletal 14 OS
117	H0Y7N4	1	0.496	Dedicator of cytokinesis protein 5 (Fragment) OS
118	P13645	18	0.485	Keratin, type I cytoskeletal 10 OS
119	B4E1C2	4	0.453	Kininogen 1, isoform CRA_b OS
120	Q0IIN1	1	0.446	Keratin 77 OS
121	B4DRR0	3	0.422	cDNA FLJ53910, highly similar to Keratin, type II cytoskeletal 6A OS
122	Q05BW3	1	0.411	NES protein (Fragment) OS
123	P13647	5	0.379	Keratin, type II cytoskeletal 5 OS
124	H6VRF8	24	0.352	Keratin 1 OS
125	P35527	16	0.270	Keratin, type I cytoskeletal 9 OS

**Table S5.B:** Differentially abundant (fold-change  $\geq 1.2$  at 1% FDR) proteins in severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis using Q-Exactive mass spectrometer

SL. No	Accession	# Unique Peptides	SVM	Description
1	P02679	11	3.390	Fibrinogen gamma chain OS
2	C9J6N2	1	2.939	Uroplakin-1b (Fragment) OS
3	Q8N5F4	1	2.923	IGL@ protein OS
4	B2R5G8	2	2.873	Serum amyloid A protein OS
5	S4R394	1	2.488	Uncharacterized protein (Fragment) OS
6	P00450	5	2.445	Ceruloplasmin OS
7	D3DQX7	2	2.433	Serum amyloid A protein OS
8	P02675	14	2.410	Fibrinogen beta chain OS
9	Q96JD0	2	2.380	Amyloid lambda 6 light chain variable region SAR (Fragment) OS
10	G3V2B9	1	2.380	Short peptide from AAT (Fragment) OS
11	Q5TEH8	1	2.283	Protein Wnt OS
12	H0YE54	1	2.282	Golgin subfamily A member 1 (Fragment) OS
13	Q9UL83	1	2.276	Myosin-reactive immunoglobulin light chain variable region (Fragment) OS
14	A8K3E4	17	2.259	cDNA FLJ78367, highly similar to Homo sapiens fibrinogen, A alpha polypeptide (FGA), transcriptvariant alpha, mRNA OS
15	P02741	5	2.227	C-reactive protein OS
16	Q5FWF9	1	2.213	IGL@ protein OS
17	P0DJI9	3	2.180	Serum amyloid A-2 protein OS
18	A2MYD2	2	2.149	V1-19 protein (Fragment) OS
19	Q4G0R1	1	2.118	PIBF1 protein OS
20	Q5NV62	2	2.019	V3-4 protein (Fragment) OS
21	B2R9V7	2	1.996	Superoxide dismutase [Cu-Zn] OS
22	P0DJI8	1	1.985	Serum amyloid A-1 protein OS
23	P02649	9	1.960	Apolipoprotein E OS
24	A2MYC8	2	1.956	V5-2 protein (Fragment) OS
25	P02790	28	1.955	Hemopexin OS
26	P01009	28	1.941	Alpha-1-antitrypsin OS
27	I1VZV6	1	1.931	Hemoglobin alpha 1 OS
28	A2JA19	1	1.913	Anti-mucin1 light chain variable region (Fragment) OS
29	P04220	2	1.882	Ig mu heavy chain disease protein OS
30	Q6ZW64	6	1.880	cDNA FLJ41552 fis, clone COLON2004478, highly similar to Protein Tro alpha1 H,myeloma OS
31	P00918	1	1.869	Carbonic anhydrase 2 OS
32	P02743	5	1.863	Serum amyloid P-component OS
33	U3PXP0	1	1.863	Alpha globin chain (Fragment) OS
34	Q5NV92	2	1.845	V5-6 protein (Fragment) OS
35	D6RF35	2	1.836	Vitamin D-binding protein OS
36	P04004	12	1.821	Vitronectin OS
37	Q9H3B5	1	1.820	PRO1367 OS
38	B2RCH7	1	1.810	cDNA, FLJ96082, highly similar to Homo sapiens cervical cancer 1 protooncogene (HCCR1), mRNA OS
39	Q9UL85	1	1.807	Myosin-reactive immunoglobulin kappa chain variable region (Fragment) OS
40	H2B4M3	1	1.786	LILRA3 protein OS
41	A0NA61	1	1.776	Codes for truncated alpha mRNA of alpha heavy chain disease patient LTE (Fragment) OS

42	B7Z570	1	1.749	cDNA FLJ53078, highly similar to Splicing factor, arginine-serine-rich 1 OS
43	P01625	3	1.734	Ig kappa chain V-IV region Len OS
44	Q3ZCV0	1	1.720	SYNE1 protein (Fragment) OS
45	P01814	1	1.720	Ig heavy chain V-II region OU OS
46	P00915	7	1.719	Carbonic anhydrase 1 OS
47	P01591	6	1.717	Immunoglobulin J chain OS
48	P00747	27	1.708	Plasminogen OS
49	P01717	2	1.682	Ig lambda chain V-IV region Hil OS
50	Q9P084	1	1.671	HSPC298 (Fragment) OS
51	Q9UL88	1	1.670	Myosin-reactive immunoglobulin heavy chain variable region (Fragment) OS
52	P06889	1	1.665	Ig lambda chain V-IV region MOL OS
53	P01008	21	1.664	Antithrombin-III OS
54	H0YCE5	1	1.664	Cyclin-dependent kinase-like 1 (Fragment) OS
55	D3DP19	1	1.660	Signal transducer and activator of transcription 4, isoform CRA_a OS
56	Q4TZM4	2	1.653	Hemoglobin beta chain (Fragment) OS
57	P06311	1	1.633	Ig kappa chain V-III region IARC/BL41 OS
58	Q8TCF0	5	1.624	LBP protein OS
59	E9PKC6	2	1.620	CD44 antigen OS
60	S6BGF9	1	1.619	IgG L chain OS
61	A2J1N0	1	1.619	Rheumatoid factor RF-IP14 (Fragment) OS
62	Q5NV91	1	1.609	V2-19 protein (Fragment) OS
63	H0Y7N4	1	1.608	Dedicator of cytokinesis protein 5 (Fragment) OS
64	A2J1N5	1	1.607	Rheumatoid factor RF-ET6 (Fragment) OS
65	Q5NV75	1	1.602	V2-15 protein (Fragment) OS
66	P02750	1	1.598	Leucine-rich alpha-2-glycoprotein OS
67	D3DPF9	2	1.591	Titin, isoform CRA_b OS
68	P01011	22	1.588	Alpha-1-antichymotrypsin OS
69	Q9UL82	2	1.579	Myosin-reactive immunoglobulin light chain variable region (Fragment) OS
70	Q5TBN3	3	1.574	Plastin-2 (Fragment) OS
71	Q6GMX6	1	1.565	IGH@ protein OS
72	A2IPI6	1	1.557	HRV Fab 027-VL (Fragment) OS
73	H0YJC8	1	1.557	Blood group Rh(CE) polypeptide (Fragment) OS
74	A2KBC6	1	1.550	Anti-FactorVIII scFv (Fragment) OS
75	P02042	4	1.542	Hemoglobin subunit delta OS
76	P02763	6	1.535	Alpha-1-acid glycoprotein 1 OS
77	O95229	1	1.532	ZW10 interactor OS
78	Q86YQ1	1	1.530	Hemoglobin alpha-2 (Fragment) OS
79	F5GX55	1	1.523	Apolipoprotein F OS
80	P02747	1	1.523	Complement C1q subcomponent subunit C OS
81	A2MYD0	2	1.510	V1-17 protein (Fragment) OS
82	S6BDG6	1	1.508	IgG L chain OS
83	Q96SA9	2	1.503	Anti-streptococcal/anti-myosin immunoglobulin kappa light chain variable region (Fragment) OS
84	A2J1M2	2	1.500	Rheumatoid factor RF-IP9 (Fragment) OS
85	I3L145	2	1.499	Sex hormone-binding globulin OS
86	B7Z549	1	0.824	cDNA FLJ56821, highly similar to Inter-alpha-trypsin inhibitor heavy chain H1 OS
87	P02766	8	0.814	Transthyretin OS
88	H0YBS8	1	0.801	Homeobox-containing protein 1 (Fragment) OS

89	Q8N506	1	0.798	ZSCAN21 protein (Fragment) OS
90	A6XND1	1	0.797	Insulin-like growth factor binding protein 3 isoform b OS
91	D3JV41	4	0.794	Thrombocidin-2 antimicrobial variant (Fragment) OS
92	H6VRF8	24	0.790	Keratin 1 OS
93	P01861	2	0.790	Ig gamma-4 chain C region OS
94	Q5SRP5	4	0.787	Apolipoprotein M OS
95	Q13789	1	0.780	Apolipoprotein B (Fragment) OS
96	B3KRK8	1	0.779	cDNA FLJ34494 fis, clone HLUNG2005030, highly similar to VIMENTIN OS
97	Q6MZU6	1	0.774	Putative uncharacterized protein DKFZp686C15213 OS
98	Q9UF98	1	0.750	Putative uncharacterized protein DKFZp434E0321 (Fragment) OS
99	P02776	3	0.746	Platelet factor 4 OS
100	Q0IIN1	1	0.731	Keratin 77 OS
101	R4GMQ4	1	0.727	Ankyrin repeat and sterile alpha motif domain-containing protein 1B (Fragment) OS
102	O00300	1	0.720	Tumor necrosis factor receptor superfamily member 11B OS
103	B4E1Q8	1	0.720	cDNA FLJ58223, highly similar to Ubiquitin ligase protein DZIP3 (EC 6.3.2.-) OS
104	E5RFX7	1	0.701	Proline synthase co-transcribed bacterial homolog protein (Fragment) OS
105	O14792	1	0.698	Heparan sulfate glucosamine 3-O-sulfotransferase 1 OS
106	B4DDH1	1	0.691	cDNA FLJ53503, highly similar to Plasma serine protease inhibitor OS
107	Q0VDD8	1	0.688	Dynein heavy chain 14, axonemal OS
108	A8MX07	1	0.672	Centrosomal protein of 19 kDa OS
109	P02652	5	0.648	Apolipoprotein A-II OS
110	Q05BW3	1	0.637	NES protein (Fragment) OS
111	D6RJG4	1	0.621	Protein kinase C zeta type OS
112	Q5VY30	6	0.605	Plasma retinol-binding protein(1-182) OS
113	K7EQB3	1	0.590	Sia-alpha-2,3-Gal-beta-1,4-GlcNAc-R:alpha 2,8-sialyltransferase (Fragment) OS
114	A8K5J7	1	0.578	cDNA FLJ77290, highly similar to Homo sapiens BCL2-associated athanogene 5 (BAG5), mRNA OS
115	A4LAA3	1	0.571	Alpha thalassemia/mental retardation syndrome X-linked OS
116	C0JYY2	135	0.569	Apolipoprotein B (Including Ag(X) antigen) OS
117	P00739	6	0.559	Haptoglobin-related protein OS
118	P06727	22	0.529	Apolipoprotein A-IV OS
119	Q8N8X9	1	0.523	Protein mab-21-like 3 OS
120	P35527	16	0.515	Keratin, type I cytoskeletal 9 OS
121	B3KXB6	1	0.490	cDNA FLJ45101 fis, clone BRAWH3032298, highly similar to Tenascin-N OS
122	C9J8U1	1	0.473	Cytospin-A (Fragment) OS
123	P02768	44	0.467	Serum albumin OS
124	P00738	13	0.459	Haptoglobin OS
125	P02647	20	0.446	Apolipoprotein A-I OS
126	P01023	75	0.429	Alpha-2-macroglobulin OS
127	Q76B58	1	0.343	BMP/retinoic acid-inducible neural-specific protein 3 OS

**Table S6.** Details of the pathways and networks associated with the differentially abundant serum proteins identified in severe and non-severe vivax malaria defined by IPA, PANTHER and DAVID analysis.

**Table S6. A:** Interaction networks associated with the differentially abundant serum proteins identified in non-severe vivax malaria defined by IPA

ID	Molecules in Network	Score	Focus Molecules	Top Diseases and Functions
1	<b>AMBP, APCS, APOA4, APOB, C1q, C1RL, chymotrypsin, CLU, CP, ERK1/2, Ferritin, FGA, GC, GLU1, HDL, HDLcholesterol, hemoglobin, HP, HPR, HPX, Iti, ITIH2, LBP, Nos, Nr1h, ORM1, SAA, SAA1, SAA2, SAA4, SERPINA1, TF, VLDL, VLDL-cholesterol, VTN</b>	50	22	Cell-To-Cell Signaling and Interaction, Tissue Development, Cancer
2	<b>A2M,Akt,ALB,C7,C1R,calpain,Collagen, Alpha1,Collagen type I,Collagen type IV,Collagen(s),Complement component 1,CRP,Cytokeratin,DPYSL2,elastase,FGB,Fibrin, Fibrinogen,HRG,Kallikrein,KNG1,KRT1,KRT2,KRT5,KRT9,KRT10,KRT14,KRT6 A,Laminin,LRG1,PLG,Stat3-Stat3,Tgf beta,VCAN,VIM</b>	39	20	Humoral Immune Response, Inflammatory Response, Inflammatory Disease
3	<b>APOA1,APOE,CA1,CFL1,CRYAB,DBI,FTH1,GOT,Growth hormone,HBA1/HBA2,HBB,HBD,HSP,Hsp27,HSPB1,IgG,IL12 (complex),Immunoglobulin,Ldh (complex),LDL,LDL-cholesterol,Mek,NADPH oxidase,NFAT (complex),NFkB(complex),PDGF BB,PEBP1,PPIA,PRDX1,PRDX2,Serine Protease,SERPINA3,Sod,SOD3,TSH</b>	36	17	Free Radical Scavenging, Hematological System Development and Function, Hematopoiesis
4	Actin, <b>AGT, aldo, ALDOA, ALDOC, Alpha, Actinin, Alpha catenin, ANXA5,Ap1,BASP1,Beta Tubulin,Calmodulin,CaMKII,Creb,FActin,FRMD5,GAP43,GAPDH,Ige,IGHM,Igm,IL1,JIN K1/2,MAP2K1/2,NEB,P38 MAPK,p70S6k,Pdgf(complex),PI3K (complex),PLC gamma,Pro-inflammatory Cytokine,Rock,S100A9,trypsin,UBC</b>	22	12	Carbohydrate Metabolism, Small Molecule Biochemistry, Cell Morphology
5	HNF1A,HNF4A,PROZ,PSMB7, <b>PZP,SERPINA10,TGFB1</b>	4	2	Cellular Development, Digestive System Development and Function, Hepatic System Development and Function
6	26s Proteasome,ADCY,caspase,CD3,Cg,chemokine,Ck 2,ERK,Focal adhesion kinase,FSH,G protein,HISTONE,Histone h3,Histone h4,Hsp70, <b>HSPA8,Iga,IgG1,Ikb,Insulin,Jnk,Mapk, Mmp,p85 (pik3r),Pkc(s),PKM,Rac,Ras,RNA polymerase II,SHBG,STAT,TCF,Tnf (family),Ubiquitin,Vegf</b>	4	3	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry

**Table S6. B:** Interaction networks associated with the differentially abundant serum proteins identified in severe vivax malaria defined by IPA

ID	Molecules in Network	Score	Focus Molecules	Top Diseases and Functions
1	<b>AMB,P,APCS,APOA2,APOA4,APOB,APOC3,C1q,CLU,CP,ERK1/2,Ferritin,FGA,GC,HDL,HDL-cholesterol,hemoglobin,HP,HPR,HPX,Iti,LBP,LRP,Nos,Nr1h,ORM1,RBP4,SAA,SAA1,SAA2,SAA4,SERPINA1,SERPINC1,VLDL,VLDL-cholesterol,VTN</b>	46	22	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry
2	<b>A2M,ALB,APOA1,APOE,CFL1,Cytokeratin,DBI,FABP5,FTH1,GOT,Growth hormone,HBB,HBD,Iga,IgG,IGH,IGHA1,IGHG1,IGJ,Igm,IL12 (complex),Immunoglobulin,KRT9,Ldh (complex),LDL,Mek,NADPH oxidase,NFkB (complex),PRDX2,Serine Protease,Sod,SOD3,TPI1,TSH,VCAN</b>	38	19	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry
3	14-3-3,Actin,Alpha Actinin,Alpha tubulin,Beta Tubulin,calpain,CaMKII,CRYAB,DPYSL2,ERK,F-Actin,Filamin,FRMD5,G-Actin,HSP,Hsp90,HSPB1,MBP,Myosin,NEB,PFN1,PPIB,Rock,SNCA,STMN1,SYN1,TCF,TMOD1,TTN,TUBA1C,TUBB3,TUBB2A,TUBB4B,tubulin (complex),tubulin (family)	32	17	Cancer, Dermatological Diseases and Conditions, Endocrine System Disorders
4	Akt,C3,C4BP,C4BPA,chymotrypsin,Collagen type I,Collagen type III,Collagen type IV,Collagen type VI,Collagen(s),Complement component 1,CRP,DDAH1,elastase,FGB,FGG,Fibrin,Fibrinogen,GPIIB-IIIa,HIST1H2BA,Integrin,Kallikrein,Laminin,LC P1,LDL-cholesterol,Lfa-1,LRG1,Mmp,NME2,P4HB,PLG,PRDX5,SERPIN A3,Stat3-Stat3,VWF	25	15	Hematological System Development and Function, Tissue Development, Inflammatory Response
5	<b>AHNAK,Alpha catenin,ANXA1,ANXA2,Ap1,BCR (complex),CA1,CA2,CA3,Calcineurin protein(s),Carbonic anhydrase,CD44,Cyclin D,FLNB,Focal adhesion kinase,GAP43,Hsp27,Ige,IGF1R,Ikb,Jnk,MAP2K1/2,Nfat (family),p70S6k,p85 (pik3r),PARP,Pdgf (complex),PDGFBB,Pkc(s),PLC gamma,Ras,Sos,TCR,Tgf beta,VIM</b>	17	11	Inflammatory Disease, Inflammatory Response, Ophthalmic Disease
6	26s Proteasome, <b>ALDH2,ALDOA,Alp,BASP1,Calmodulin,Cg,Ck2,Creb,DNAH10,DNAH11,estrogen receptor,Gsk3,HISTONE,Hsp70,HSPA5,IL1,IL12 (family),Insulin,LGALS3BP,Lh,Mapk,MHC Class II (complex),P38 MAPK,PGK1,PI3K (complex),Pka,Pro-inflammatory Cytokine,Proinsulin,SRC(family),Tnf (family),trypsin,Ubiquitin,UCHL1,YWHAH</b>	16	10	Hematological Disease, Immunological Disease, Inflammatory Disease

7	CAMSAP2,caspase,CD3,chemokine,CHIA, <b>CMBL</b> ,CUL2,ELANE, <b>ENPP6</b> ,FAM98B,FN1, <b>HIST1H2A D</b> ,HIST1H4D,HIST1H4K,HIST1H4L, <b>HNRNPA1</b> , <b>HNRNPA2B1</b> ,HNRPA1-HNRPA2B1-POT1-TERF1- TERF2, <b>IGHA2</b> ,MIR320,MRPL13,PKD1, <b>POTEE/POTEF</b> ,PRPF39,Rac,RBM12,RNF187, <b>RPLP0</b> ,SD F2,SETBP1,SFI1,SUMO1,Tra@-Trb@,Vegf,ZNF711	12	8	Connective Tissue Disorders, Developmental Disorder, Hereditary Disorder
8	AEBP1,Ahr-arylhydrocarbon-Arnt,AOC1,asialo GM1 ganglioside,cerebroside 3-sulfate,CLCF1,ERK1/2,FAIM3,FEZF1,FPR2,FUT 8,HAS1,IFITM3,IFNL2,IgG1,IL19,IL20,IL21R,JA M2,LRRN1,mir-150,MPL,MUC5B,PDGFC,PHLDA2,Pki,Pvr,RAS GRP3,SP1,STAT,TACSTD2, <b>TIMELESS</b> ,TNFSF8 ,TREX1,TRIB1	1	1	Humoral Immune Response, Protein Synthesis, Cellular Growth and Proliferation

Bold candidates are differentially abundant proteins in *vivax* malaria identified in this study

**Table S6. C:** Pathways associated with the differentially abundant serum proteins identified in non-severe vivax malaria defined by IPA

S.I. No	Ingenuity canonical pathway	-log( <i>p</i> -value)	Ratio	Molecules
1	Acute phase Response signaling	30.639	0.142	P01023,P02768,P02760,P02743,P02647,P00450,P02741,P02671,P02675,P00738,P02790,P04196,P19823,P02763,P00747,P0DJ18,P0DJI9,B2R5G8,P01009,P01011
2	LXR/RXR Activation Molecule	28.647	0.174	P02768,P02760,P02647,P06727,C0JYY2,P02649,P10909,P02671,P00739,P02790,B4E1C2,P18428,P02763,P0DJI8,P0DJI9,B2R5G8,P01009, P04004
3	FXR/RXR Activation Molecules	26.349	0.152	P02768,P02760,P02647,P06727,C0JYY2,P02649,P10909,P02671,P00739,P02790,B4E1C2,P02763,P0DJI8,P0DJI9,B2R5G8,P01009, P04004
4	Clatrin-mediated Endocytosis Signaling	11.082	0.065	P02768,P02647,P06727,C0JYY2,P02649,P10909,P11142,P02763,B2R5G8,P01009, P0CG48
5	Atherosclerosis Signaling Pathway	8.866	0.073	P02768,P02647,P06727,C0JYY2,P02649,P10909,P02763,B2R5G8,P01009
6	IL-12 signaling and production in Macrophages molecules	8.506	0.067	P02768,P02647,P06727,C0JYY2,P02649,P10909,P02763,B2R5G8,P01009
7	Coagulation System	8.327	0.171	P01023,P02671,P02675, P00747,P01009
8	Production of nitric oxide and reactive oxygen species in macrophages	7.414	0.05	P02768,P02647,P06727,C0JYY2,P02649,P10909,P02763,B2R5G8,P01009
9	NRF-2 mediated oxidative stress response	1.459	0.017	B2R9V7

**Table S6. D:** Pathways associated with the differentially abundant serum proteins identified in severe vivax malaria defined by IPA

S.I. No	Ingenuity canonical pathway	-log(p-value)	Ratio	Molecules
1	Acute phase Response signaling	28.784	0.148	P01023, P02768,P02760,P02743,P02647,P0736,P00450,P02741P02671,P02675,P00738,P02790, P19823,P02763,P00747,P0DJI8,P0DJI9,B2R5G8,P01009,P01011,
2	Atherosclerosis Signaling Pathway	11.63	0.098	P02768,P02647,P02652,P06727,C0JYY2, P02649, P10909,P02763,Q5VY30,B2R5G8,P01009
3	Coagulation System	10.993	0.229	P01023,A8K3E4,P02675,P02679,P00747,P01009,P01008
4	FXR/RXR Activation Molecules	25.158	0.165	P02768,P02760,P02647,P02652,P06727,C0JYY2,P02656,P02649,P01024,P10909,A8K3E4, P0739,P02790,P02763,Q5VY30,P0DJI8,B2R5G8,P01009,P04004
5	IL-12 signaling and production in Macrophages molecules	11.146	0.0897	P02768,P02647,P02652,P06727,C0JYY2, P02649, P10909,P02763,Q5VY30,B2R5G8,P01009
6	LXR/RXR Activation Molecule	27.368	0.1824	P02768,P02760,P02647,P06727,C0JYY2,P02649,P10909,P02671, P00739,P02790,B4E1C2, P02763,P0DJI8,P0DJI9,B2R5G8,P01009, P04004
7	Production of nitric oxide and reactive oxygen species in macrophages	9.676	0.067	P02768,P02647,P02652,P06727,C0JYY2,P02649, P10909,P02763,Q5VY30,B2R5G8,P01009
8	Actin cytoskeleton signaling	1.542	0.018	Q8TCF0,P07737,Q8WZ42
9	Gap junction signaling	2.023	0.026	Q9BQE3,Q13509,P68371
10	Axonal guidance signaling	2.081	0.016	Q16555,P07737,Q9BQE3,Q13509,Q13885, P68371

**Table S6. E:** Pathways associated with the differentially abundant serum proteins identified in severe vivax malaria defined by DAVID

Category	Term	Count	%	p-Value	Gene	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FD
BBID	Integrins and other cell-surface receptors	2	3.70	0.07141	Q8TCF0, P08571	3	13	358	18.35	0.35	0.35	29.85
KEGG PATHWAY	Complement and coagulation cascades	4	7.41	0.00142	P05155, P05156, P01009, P00747	18	69	5085	16.37	0.04	0.04	1.18
PANTHER PATHWAY	Inflammation mediated by chemokine and cytokine signaling pathway	3	5.56	0.09084	O14921, Q8WZ42, P35354	6	304	2857	4.7	0.5332	0.5332	40.629 7
PANTHER PATHWAY	Blood coagulation	2	3.70	0.09268	P01009, P00747	6	55	2857	17.31	0.540	0.32	41.28
REACTOME PATHWAY	Hemostasis	9	16.67	1.80E-05	P04114, P05155, P02768, P00441, Q8WZ42, P10909, P01009, P00747, P02647	20	235	3398	6.507	0.0003	0.0003	0.013
REACTOME PATHWAY	Metabolism of lipids and lipoproteins	6	11.11	0.00110	P04114, P02649, P02768, P06727, P02652, P02647	20	150	3398	6.796	0.0197	0.0099	0.8103

**Table S6. E:** Pathways associated with the differentially abundant serum proteins identified in non-severe vivax malaria defined by DAVID

Category	Term	Count	%	P-Value	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
KEGG PATHWAY	Complement and coagulation cascades	5	15.15	9.54E-06	P02671, P05156, P01009, P00747, P00734	12	69	5085	30.70	1.53E-04	1.53E-04	0.0067
BIOCARTA	Fibrinolysis Pathway	3	9.09	0.0010	P02671, P00747, P00734	8	11	1437	48.98	0.01739	0.0173	0.7758
BIOCARTA	Acute Myocardial Infarction	3	9.09	0.0015	P02671, P00747, P00734	8	13	1437	41.45	0.0244	0.0123	1.0937
BIOCARTA	Platelet Amyloid Precursor Protein Pathway	2	6.06	0.0431	P00747, P00734	8	9	1437	39.91	0.5059	0.2094	26.872
BIOCARTA	Extrinsic Prothrombin Activation Pathway	2	6.06	0.0524	P02671, P00734	8	11	1437	32.65	0.5778	0.1939	31.8039
BIOCARTA	Intrinsic Prothrombin Activation Pathway	2	6.06	0.080	P02671, P00734	8	17	1437	21.13	0.7370	0.2344	44.723
PANTHER PATHWAY	Blood coagulation	4	12.12	2.67E-05	P02671, P01009, P00747, P00734	5	55	2857	41.55	8.00E-05	8.00E-05	0.0083
PANTHER PATHWAY	Plasminogen activating cascade	2	6.06	0.030	P02671, P00747	5	22	2857	51.94	0.0886	0.0453	9.2795
REACTOME PATHWAY	Hemostasis	8	24.24	8.30E-06	P02671, P02768, P00441, P10909, P01009, P00747, P00734, P02647	14	235	3398	8.26	1.16E-04	1.16E-04	0.00564
REACTOME PATHWAY	Metabolism of lipids and lipoproteins	4	12.12	0.0174	P02649, P02768, P06727, P02647	14	150	3398	6.47	0.2172	0.11563	11.2413

**Table S6.G:** Pathways associated with the differentially abundant serum proteins identified in severe vivax malaria defined by PANTHER

	Total list	Count	Expected	+/-	P-value
<b>Pathways</b>					
Toll receptor signaling pathway (P00054)	56	3	0.15	+	4.36E-04
Blood coagulation (P00011)	51	2	0.13	+	7.89E-03
Endothelin signaling pathway (P00019)	87	2	0.23	+	2.17E-02
Inflammation mediated by chemokine and cytokine signaling pathway	245	3	0.64	+	2.59E-02
<b>Molecular Function</b>					
Antioxidant activity (GO:0016209)	30	2	0.08	+	2.83E-03
Lipid transporter activity (GO:0005319)	112	5	0.29	+	1.15E-05
Lipid binding (GO:0008289)	73	3	0.19	+	9.36E-04
Peptidase inhibitor activity (GO:0030414)	226	8	0.59	+	1.29E-07
Calcium-dependent phospholipid binding (GO:0005544)	139	4	0.36	+	4.82E-04
Enzyme activator activity (GO:0008047)	139	4	0.36	+	4.82E-04
Serine-type peptidase activity (GO:0008236)	322	8	0.84	+	1.81E-06
Enzyme inhibitor activity (GO:0004857)	362	8	0.94	+	4.27E-06
Lipase activity (GO:0016298)	92	2	0.24	+	2.40E-02
Hormone activity (GO:0005179)	161	3	0.42	+	8.56E-03
Transferase activity, transferring acyl groups (GO:0016746)	179	3	0.46	+	1.14E-02
Peptidase activity (GO:0008233)	630	9	1.63	+	3.30E-05
Calmodulin binding (GO:0005516)	282	4	0.73	+	6.22E-03
Enzyme regulator activity (GO:0030234)	1002	13	2.6	+	1.28E-06
Calcium ion binding (GO:0005509)	449	4	1.16	+	2.92E-02
Oxidoreductase activity (GO:0016491)	626	5	1.62	+	2.30E-02
Receptor binding (GO:0005102)	980	7	2.54	+	1.30E-02
Hydrolase activity (GO:0016787)	2205	14	5.72	+	1.19E-03
Catalytic activity (GO:0003824)	5209	20	13.51	+	3.37E-02
<b>Biological Process</b>					
Cell growth (GO:0016049)	3	1	0.01	+	7.75E-03
Growth (GO:0040007)	5	1	0.01	+	1.29E-02
Vitamin transport (GO:0051180)	59	3	0.15	+	5.07E-04
Fatty acid biosynthetic process (GO:0006633)	42	2	0.11	+	5.43E-03
Complement activation (GO:0006956)	45	2	0.12	+	6.21E-03
Cholesterol metabolic process (GO:0008203)	83	3	0.22	+	1.35E-03
Lipid transport (GO:0006869)	322	8	0.84	+	1.81E-06
Blood circulation (GO:0008015)	154	3	0.4	+	7.58E-03
Cell differentiation (GO:0030154)	161	3	0.42	+	8.56E-03
Blood coagulation (GO:0007596)	168	3	0.44	+	9.60E-03
Anion transport (GO:0006820)	173	3	0.45	+	1.04E-02
Steroid metabolic process (GO:0008202)	179	3	0.46	+	1.14E-02
Cellular component biogenesis (GO:0044085)	310	5	0.8	+	1.26E-03
Homeostatic process (GO:0042592)	209	3	0.54	+	1.72E-02
Response to external stimulus (GO:0009605)	378	5	0.98	+	2.98E-03
Regulation of catalytic activity (GO:0050790)	1073	13	2.78	+	2.72E-06
Regulation of molecular function (GO:0065009)	1096	13	2.84	+	3.44E-06

Response to stress (GO:0006950)	659	7	1.71	+	1.53E-03
Catabolic process (GO:0009056)	407	4	1.06	+	2.13E-02
Lipid metabolic process (GO:0006629)	880	7	2.28	+	7.48E-03
Proteolysis (GO:0006508)	719	5	1.87	+	3.84E-02
System process (GO:0003008)	1296	8	3.36	+	1.80E-02
Response to stimulus (GO:0050896)	2170	12	5.63	+	8.65E-03
Single-multicellular organism process (GO:0044707)	1636	9	4.24	+	2.40E-02
Multicellular organismal process (GO:0032501)	1640	9	4.25	+	2.44E-02
Localization (GO:0051179)	2607	14	6.76	+	5.66E-03
Transport (GO:0006810)	2473	13	6.42	+	9.34E-03
Unclassified (UNCLASSIFIED)	8629	14	22.39	-	1.31E-02
Cell communication (GO:0007154)	3006	2	7.8	-	1.12E-02
<b>Cellular Component</b>					
Extracellular space (GO:0005615)	6	3	0.02	+	5.88E-07
Extracellular region (GO:0005576)	662	15	1.72	+	9.19E-11
Extracellular matrix (GO:0031012)	259	4	0.67	+	4.62E-03
Macromolecular complex (GO:0032991)	849	6	2.2	+	2.23E-02
Unclassified (UNCLASSIFIED)	16726	32	43.39	-	2.99E-04
<b>Protein Class</b>					
Serine protease inhibitor (PC00204)	119	5	0.31	+	1.53E-05
Apolipoprotein (PC00052)	84	3	0.22	+	1.40E-03
Protease inhibitor (PC00191)	245	8	0.64	+	2.37E-07
Annexin (PC00050)	168	4	0.44	+	9.73E-04
Transfer/carrier protein (PC00219)	400	8	1.04	+	8.80E-06
Peptide hormone (PC00179)	165	3	0.43	+	9.14E-03
Antibacterial response protein (PC00051)	126	2	0.33	+	4.26E-02
Serine protease (PC00203)	287	4	0.74	+	6.61E-03
Intracellular calcium-sensing protein (PC00131)	304	4	0.79	+	8.06E-03
Calmodulin (PC00061)	304	4	0.79	+	8.06E-03
Defense/immunity protein (PC00090)	551	6	1.43	+	2.99E-03
Extracellular matrix protein (PC00102)	380	4	0.99	+	1.70E-02
Calcium-binding protein (PC00060)	400	4	1.04	+	2.01E-02
Cell adhesion molecule (PC00069)	507	5	1.32	+	1.01E-02
Enzyme modulator (PC00095)	1346	11	3.49	+	5.88E-04
Protease (PC00190)	508	4	1.32	+	4.28E-02
Unclassified (UNCLASSIFIED)	9675	18	25.1	-	3.48E-02

**Table S6.H:** Pathways associated with the differentially abundant serum proteins identified in non-severe vivax malaria defined by PANTHER

	Total list	Count	Expected	+/-	P-value
<b>PANTHER Pathways</b>					
Plasminogen activating cascade (P00050)	21	2	0.04	+	5.92E-04
Blood coagulation (P00011)	51	4	0.09	+	1.78E-06
<b>Molecular Function</b>					
Lipid binding (GO:0008289)	73	3	0.12	+	2.60E-04
Lipid transporter activity (GO:0005319)	112	4	0.19	+	3.84E-05
Antioxidant activity (GO:0016209)	30	1	0.05	+	4.92E-02
Calcium-dependent phospholipid binding (GO:0005544)	139	4	0.23	+	8.83E-05
Peptidase inhibitor activity (GO:0030414)	226	6	0.38	+	2.03E-06
Serine-type peptidase activity (GO:0008236)	322	8	0.54	+	5.32E-08
Hormone activity (GO:0005179)	161	4	0.27	+	1.55E-04
Lipase activity (GO:0016298)	92	2	0.15	+	1.06E-02
Enzyme activator activity (GO:0008047)	139	3	0.23	+	1.66E-03
Transferase activity, transferring acyl groups (GO:0016746)	179	3	0.3	+	3.39E-03
Enzyme inhibitor activity (GO:0004857)	362	6	0.61	+	2.91E-05
Calmodulin binding (GO:0005516)	282	4	0.47	+	1.26E-03
Peptidase activity (GO:0008233)	630	8	1.06	+	7.97E-06
Calcium ion binding (GO:0005509)	449	5	0.76	+	8.84E-04
Enzyme regulator activity (GO:0030234)	1002	10	1.68	+	4.03E-06
Receptor binding (GO:0005102)	980	8	1.65	+	1.81E-04
Hydrolase activity (GO:0016787)	2205	12	3.71	+	1.59E-04
Catalytic activity (GO:0003824)	5209	14	8.76	+	3.66E-02
<b>Biological Process</b>					
Cell growth (GO:0016049)	3	1	0.01	+	5.03E-03
Growth (GO:0040007)	5	1	0.01	+	8.37E-03
Complement activation (GO:0006956)	45	3	0.08	+	6.28E-05
Fatty acid biosynthetic process (GO:0006633)	42	2	0.07	+	2.32E-03
Cholesterol metabolic process (GO:0008203)	83	3	0.14	+	3.77E-04
Vitamin transport (GO:0051180)	59	2	0.1	+	4.49E-03
Blood circulation (GO:0008015)	154	5	0.26	+	5.98E-06
Locomotion (GO:0040011)	65	2	0.11	+	5.42E-03
Blood coagulation (GO:0007596)	168	5	0.28	+	9.09E-06
Lipid transport (GO:0006869)	322	8	0.54	+	5.32E-08
Response to external stimulus (GO:0009605)	378	8	0.64	+	1.80E-07
Cell differentiation (GO:0030154)	161	3	0.27	+	2.52E-03
Anion transport (GO:0006820)	173	3	0.29	+	3.08E-03
Steroid metabolic process (GO:0008202)	179	3	0.3	+	3.39E-03
Homeostatic process (GO:0042592)	209	3	0.35	+	5.21E-03
Response to stress (GO:0006950)	659	9	1.11	+	1.07E-06
Phospholipid metabolic process (GO:0006644)	182	2	0.31	+	3.76E-02
Fatty acid metabolic process (GO:0006631)	202	2	0.34	+	4.54E-02
Catabolic process (GO:0009056)	407	4	0.68	+	4.72E-03

Cellular component biogenesis (GO:0044085)	310	3	0.52	+	1.52E-02
Regulation of catalytic activity (GO:0050790)	1073	10	1.8	+	7.38E-06
Regulation of molecular function (GO:0065009)	1096	10	1.84	+	8.89E-06
Gamete generation (GO:0007276)	351	3	0.59	+	2.10E-02
Proteolysis (GO:0006508)	719	6	1.21	+	1.16E-03
Lipid metabolic process (GO:0006629)	880	7	1.48	+	5.70E-04
Cell-cell adhesion (GO:0016337)	391	3	0.66	+	2.77E-02
Reproduction (GO:0000003)	410	3	0.69	+	3.13E-02
System process (GO:0003008)	1296	9	2.18	+	2.25E-04
Response to stimulus (GO:0050896)	2170	15	3.65	+	7.83E-07
Cellular component movement (GO:0006928)	476	3	0.8	+	4.55E-02
Single-mitochondrial organism process (GO:0044707)	1636	10	2.75	+	2.63E-04
Mitochondrial organismal process (GO:0032501)	1640	10	2.76	+	2.68E-04
Localization (GO:0051179)	2607	15	4.38	+	7.94E-06
Transport (GO:0006810)	2473	13	4.16	+	1.08E-04
Nervous system development (GO:0007399)	823	4	1.38	+	4.83E-02
Immune system process (GO:0002376)	1391	6	2.34	+	2.71E-02
Protein metabolic process (GO:0019538)	2692	9	4.53	+	3.06E-02
Unclassified (UNCLASSIFIED)	8629	8	14.51	-	1.72E-02
<b>Cellular Component</b>					
Extracellular space (GO:0005615)	6	3	0.01	+	1.56E-07
Extracellular region (GO:0005576)	662	14	1.11	+	1.34E-12
Macromolecular complex (GO:0032991)	849	5	1.43	+	1.32E-02
Unclassified (UNCLASSIFIED)	16726	16	28.13	-	5.64E-06
<b>Protein Class</b>					
Complement component (PC00078)	51	2	0.09	+	3.39E-03
Apolipoprotein (PC00052)	84	3	0.14	+	3.91E-04
Protease inhibitor (PC00191)	245	6	0.41	+	3.22E-06
Peptide hormone (PC00179)	165	4	0.28	+	1.70E-04
Annexin (PC00050)	168	4	0.28	+	1.82E-04
Serine protease (PC00203)	287	6	0.48	+	7.91E-06
Transfer/carrier protein (PC00219)	400	7	0.67	+	4.06E-06
Serine protease inhibitor (PC00204)	119	2	0.2	+	1.72E-02
Antibacterial response protein (PC00051)	126	2	0.21	+	1.91E-02
Intracellular calcium-sensing protein (PC00131)	304	4	0.51	+	1.66E-03
Calmodulin (PC00061)	304	4	0.51	+	1.66E-03
Defense/immunity protein (PC00090)	551	7	0.93	+	3.19E-05
Calcium-binding protein (PC00060)	400	5	0.67	+	5.26E-04
Protease (PC00190)	508	6	0.85	+	1.87E-04
Signaling molecule (PC00207)	1083	6	1.82	+	8.75E-03
Enzyme modulator (PC00095)	1346	7	2.26	+	6.37E-03
Hydrolase (PC00121)	1511	7	2.54	+	1.17E-02
Receptor (PC00197)	1596	7	2.68	+	1.55E-02
Unclassified (UNCLASSIFIED)	9675	10	16.27	-	2.38E-02

**Table S7.** ELISA-based measurement of serum proteins in healthy community controls, severe and non-severe vivax malaria, dengue fever and leptospirosis patients

A. ELISA-based measurement of Apolipoprotein A-I (Apo A-I)

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	0.06	0.00	0.01	0.09	0.44
25% Percentile	0.72	0.24	0.16	0.44	0.61
Median	1.05	0.46	0.36	0.72	0.75
75% Percentile	1.45	0.79	0.70	1.32	1.08
Maximum	2.56	1.45	1.22	1.61	1.75
Mean	1.10	0.54	0.48	0.81	0.85
Std. Deviation	0.54	0.38	0.38	0.47	0.38
Std. Error of Mean	0.06	0.04	0.08	0.11	0.11
Lower 95% CI of mean	0.99	0.47	0.32	0.59	0.61
Upper 95% CI of mean	1.21	0.62	0.63	1.03	1.09

B. ELISA-based measurement of Apolipoprotein E (Apo E)

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	42.89	44.09	62.15	49.63	68.48
25% Percentile	86.88	114.05	154.30	84.64	106.96
Median	112.58	167.75	214.07	165.26	122.16
75% Percentile	139.27	214.85	363.04	193.31	145.45
Maximum	239.66	379.91	623.00	276.61	177.98
Mean	113.95	171.97	255.19	150.05	125.36
Std. Deviation	38.65	74.86	158.65	72.18	34.46
Std. Error of Mean	4.01	7.56	31.11	16.14	9.95
Lower 95% CI of mean	105.99	156.96	191.11	116.27	103.46
Upper 95% CI of mean	121.91	186.98	319.27	183.84	147.26

C. ELISA-based measurement of Ceruloplasmin (CP)

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	0.18	0.15	0.25	0.20	0.29
25% Percentile	0.25	0.33	0.39	0.26	0.38
Median	0.32	0.45	0.67	0.34	0.46
75% Percentile	0.41	0.62	1.00	0.42	0.66
Maximum	0.64	1.30	1.55	0.61	0.72
Mean	0.35	0.49	0.74	0.36	0.49
Std. Deviation	0.13	0.21	0.41	0.13	0.15
Std. Error of Mean	0.02	0.03	0.08	0.03	0.04
Lower 95% CI of mean	0.32	0.43	0.57	0.30	0.40
Upper 95% CI of mean	0.39	0.55	0.90	0.42	0.59

**D. ELISA-based measurement of Haptoglobin (HP)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	0.06	0.00	0.00	0.27	0.12
25% Percentile	0.66	0.27	0.03	1.04	0.76
Median	0.97	0.41	0.20	1.36	1.50
75% Percentile	1.35	0.62	0.38	1.88	1.71
Maximum	2.25	1.52	1.91	2.88	2.16
Mean	1.02	0.48	0.39	1.48	1.31
Std. Deviation	0.49	0.31	0.53	0.67	0.60
Std. Error of Mean	0.05	0.03	0.08	0.13	0.17
Lower 95% CI of mean	0.92	0.42	0.23	1.21	0.93
Upper 95% CI of mean	1.11	0.53	0.56	1.75	1.68

**E. ELISA-based measurement of Hemophrin (HPX)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	0.36	0.46	0.66	0.42	0.52
25% Percentile	0.89	1.03	1.33	0.99	0.85
Median	1.18	1.30	1.98	1.29	1.52
75% Percentile	1.44	1.61	2.37	1.82	1.76
Maximum	2.20	2.51	2.94	2.33	2.18
Mean	1.18	1.33	1.85	1.37	1.39
Std. Deviation	0.41	0.41	0.66	0.52	0.53
Std. Error of Mean	0.04	0.04	0.13	0.12	0.15
Lower 95% CI of mean	1.10	1.24	1.58	1.13	1.05
Upper 95% CI of mean	1.27	1.41	2.11	1.61	1.72

**F. ELISA-based measurement of Retinol binding protein 4 (RBP4)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	11.43	11.06	6.90	12.97	13.30
25% Percentile	29.85	25.99	18.45	31.67	41.46
Median	37.02	33.50	25.44	41.06	45.09
75% Percentile	49.19	42.78	32.01	48.71	59.20
Maximum	87.34	64.18	47.86	66.29	67.35
Mean	40.06	34.50	25.91	39.68	45.19
Std. Deviation	14.55	13.03	11.03	12.81	16.52
Std. Error of Mean	1.51	1.32	2.16	2.86	4.77
Lower 95% CI of mean	37.06	31.88	21.46	33.68	34.70
Upper 95% CI of mean	43.05	37.11	30.36	45.67	55.69

**G. ELISA-based measurement of Plasminogen (PLS)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	1.15	1.09	1.56	1.67	1.28
25% Percentile	1.62	1.90	2.04	1.90	1.59
Median	1.89	2.44	3.56	2.80	2.45
75% Percentile	2.15	3.56	4.29	3.21	3.38
Maximum	2.89	4.28	5.19	3.56	3.78
Mean	1.91	2.63	3.33	2.65	2.48
Std. Deviation	0.48	0.96	1.25	0.68	0.97
Std. Error of Mean	0.13	0.27	0.40	0.24	0.43
Lower 95% CI of mean	1.62	2.05	2.43	2.08	1.28
Upper 95% CI of mean	2.20	3.21	4.22	3.22	3.67

**H. ELISA-based measurement of Serum amyloid A (SAA)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>	<b>LEP</b>
Minimum	0.02	0.54	3.58	2.92	0.42
25% Percentile	0.39	12.46	15.34	7.96	2.92
Median	1.05	30.43	63.13	23.51	8.91
75% Percentile	3.23	83.93	201.99	56.66	29.57
Maximum	100.14	1188.67	1668.89	179.90	128.54
Mean	4.39	80.64	183.51	38.77	24.13
Std. Deviation	11.53	154.27	318.69	41.52	37.73
Std. Error of Mean	1.14	14.20	49.18	8.14	10.89
Lower 95% CI of mean	2.13	52.51	84.20	22.00	0.16
Upper 95% CI of mean	6.64	108.76	282.82	55.54	48.11

**I. ELISA-based measurement of Vitronectin (VTN)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>
Minimum	368.42	390.58	427.92
25% Percentile	418.815	423.497	459.48
Median	443.02	474.875	530.96
75% Percentile	471.9	509.742	600.94
Maximum	517.58	528.41	615.32
Mean	445.538	467.576	523.874
Std. Deviation	42.4624	45.7541	69.1436
Std. Error of Mean	12.2578	14.4687	21.8651
Lower 95% CI of mean	418.559	434.845	474.411
Upper 95% CI of mean	472.516	500.307	573.337

**J. ELISA-based measurement of serum Superoxide dismutase (SOD)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>
Minimum	4.225	4.195	4.505
25% Percentile	4.59525	4.44225	5.54925
Median	4.78	4.6635	6.528
75% Percentile	5.1555	5.1735	8.47275
Maximum	5.727	5.913	26.797
Mean	4.9045	4.77975	8.35515
Std. Deviation	0.439803	0.460256	5.12153
Std. Error of Mean	0.109951	0.102916	1.14521
Lower 95% CI of mean	4.67015	4.56434	5.95817
Upper 95% CI of mean	5.13885	4.99516	10.7521

**K. ELISA-based measurement of Titin (TTN)**

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>
Minimum	10.75	14	28
25% Percentile	14.5	20.5	35.75
Median	28.25	30	63.125
75% Percentile	39.5	66	88
Maximum	43.25	90	94
Mean	27.4167	40.25	63
Std. Deviation	14.0238	27.4109	25.3937
Std. Error of Mean	5.72519	9.69121	7.33053
Lower 95% CI of mean	12.6996	17.3336	46.8658
Upper 95% CI of mean	42.1338	63.1664	79.1342

**Table S8:** Statistical summary of ROC curve analysis for evaluating performance of different serum proteins for prediction of non-severe and severe vivax malaria

Classifier protein	HC vs. NSVM		HC vs. SVM		NSVM vs. SVM	
	AUC	95% CI	AUC	95% CI	AUC	95% CI
Apolipoprotein A-I	0.799	0.736 to 0.861	0.825	0.742 to 0.908	0.557	0.427 to 0.688
Apolipoprotein E	0.747	0.675 to 0.818	0.811	0.683 to 0.938	0.656	0.521 to 0.791
Cerruloplasmin	0.71	0.610 to 0.810	0.821	0.715 to 0.928	0.678	0.542 to 0.815
Haptoglobin	0.818	0.760 to 0.876	0.83	0.740 to 0.919	0.688	0.577 to 0.800
Hemopexin	0.594	0.514 to 0.675	0.789	0.667 to 0.911	0.731	0.593 to 0.870
Plasminogen	0.736	0.535 to 0.938	0.826	0.637 to 1.01	0.661	0.426 to 0.896
Retinol binding protein 4	0.602	0.523 to 0.682	0.788	0.689 to 0.887	0.687	0.576 to 0.798
Serum amyloid A	0.931	0.898 to 0.963	0.959	0.931 to 0.986	0.609	0.505 to 0.714
Titin	0.625	0.3115 to 0.9385	0.875	0.7091 to 1.041	0.75	0.5168 to 0.9832
Vitronectin	0.65	0.4102 to 0.8898	0.825	0.6442 to 1.006	0.76	0.5391 to 0.9809
Superoxide dismutase	0.6094	0.4200 to 0.7988	0.8844	0.7688 to 0.9999	0.9088	0.8172 to 1.000

**Table S9.** Calibration-free concentration analysis (CFCA) for serum amyloid A (SAA) in serum samples of healthy community controls, non-severe and severe vivax malaria, and dengue fever patients

A. Measurement of SAA in pooled samples

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>
25% Percentile	6	6	6	6
Median	6.4	20	24	8.5
75% Percentile	7	20.75	24.75	9.325
Maximum	8.35	21	25	9.7
Mean	9.875	22	25.25	10.25
Std. Deviation	11	22	26	11
Std. Error of Mean	8.46667	21.1667	25	9.75
Lower 95% CI of mean	1.65126	0.752773	0.632456	0.804363
Upper 95% CI of mean	0.674125	0.307318	0.258199	0.32838

B. Measurement of SAA in individual samples

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>	<b>DF</b>
25% Percentile	14	14	14	16
Median	7	14	16	7.3
75% Percentile	8.65	19	22.75	7.525
Maximum	11	25	25	11
Mean	12	25.75	33	13
Std. Deviation	15	30	38	30
Std. Error of Mean	10.6357	23.3571	26.7857	11.5437
Lower 95% CI of mean	2.45689	4.53376	6.55367	5.64954
Upper 95% CI of mean	0.656632	1.2117	1.75154	1.41238

**Table S10.** Measurement of superoxide dismutase (SOD) activity in healthy community controls, non-severe and severe vivax malaria patients

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>
Minimum	0.059846	0.622007	1.23673
25% Percentile	0.673499	0.803713	1.29949
Median	0.781011	1.06582	1.79595
75% Percentile	0.922821	1.39136	1.93857
Maximum	1.05667	1.62955	2.76971
Mean	0.736907	1.11162	1.76317
Std. Deviation	0.302802	0.34096	0.500239
Std. Error of Mean	0.107057	0.120547	0.176861
Lower 95% CI of mean	0.483755	0.826564	1.34495
Upper 95% CI of mean	0.990059	1.39667	2.18138

**Table S11.** Measurement of serum levels of thiobarbituric acid reactive substances (TBARS) in healthy community controls, non-severe and severe vivax malaria patients

	<b>HC</b>	<b>NSVM</b>	<b>SVM</b>
Minimum	15.2031	30.1118	23.2733
25% Percentile	25.9339	30.7331	25.3115
Median	29.5089	32.5518	45.7825
75% Percentile	34.2197	35.9435	54.798
Maximum	34.6225	41.0692	58.6322
Mean	28.7439	33.5009	41.8239
Std. Deviation	6.42323	3.71618	14.1453
Std. Error of Mean	2.27096	1.31387	5.00112
Lower 95% CI of mean	23.3738	30.394	29.998
Upper 95% CI of mean	34.1139	36.6077	53.6498

## B. Supplementary Figures

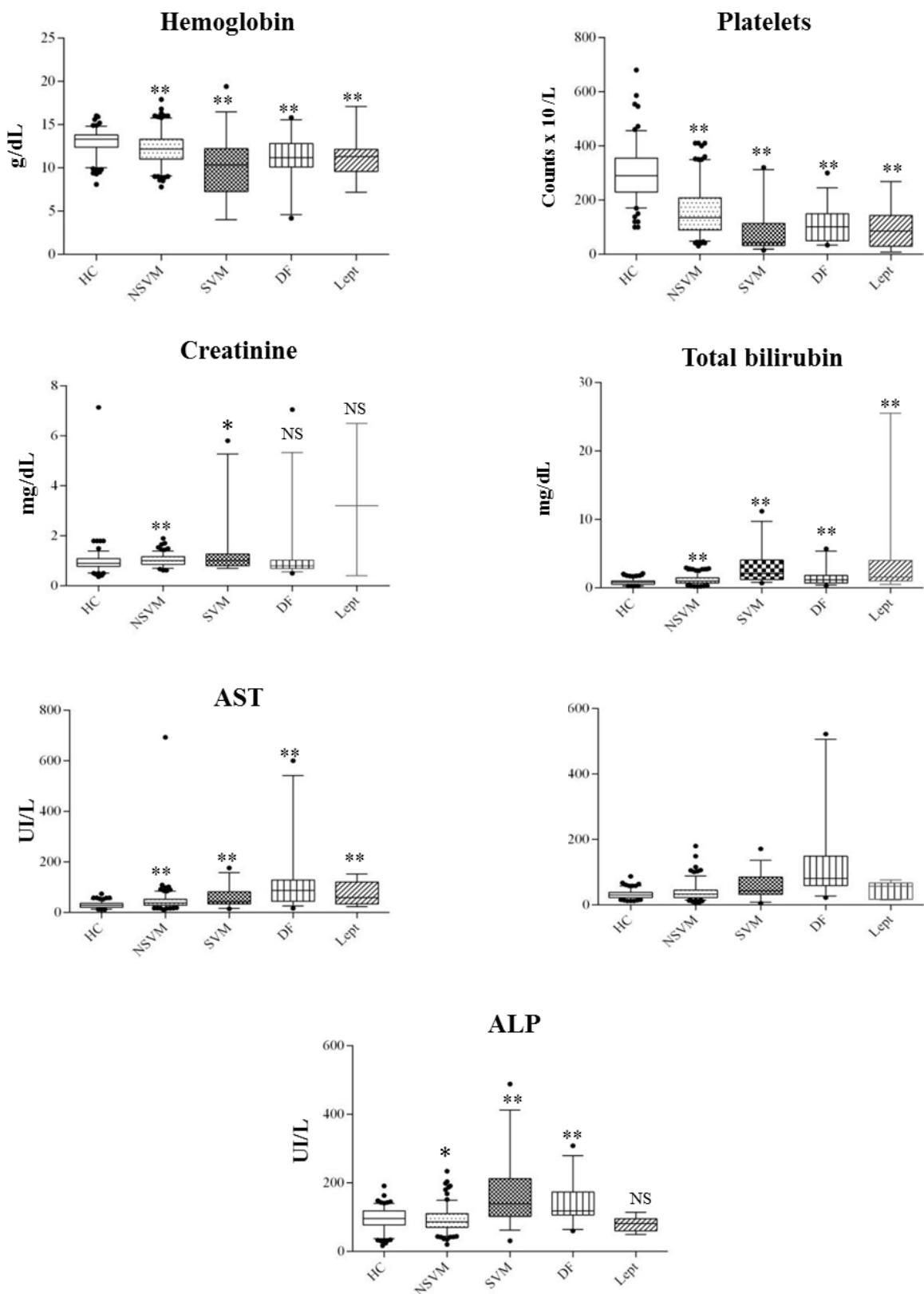
**Figure S1.** Analysis of clinicopathological parameters in healthy community controls, non-severe and severe vivax malaria, dengue fever and leptospirosis patients.

**Figure S2.** (A) Distribution of the differentially abundant proteins in severe and non-severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis (Q-TOF and Q-Exactive) (B) Scatter plots exhibiting correlations among the different iTRAQ data sets (analyzed by using Q-TOF).

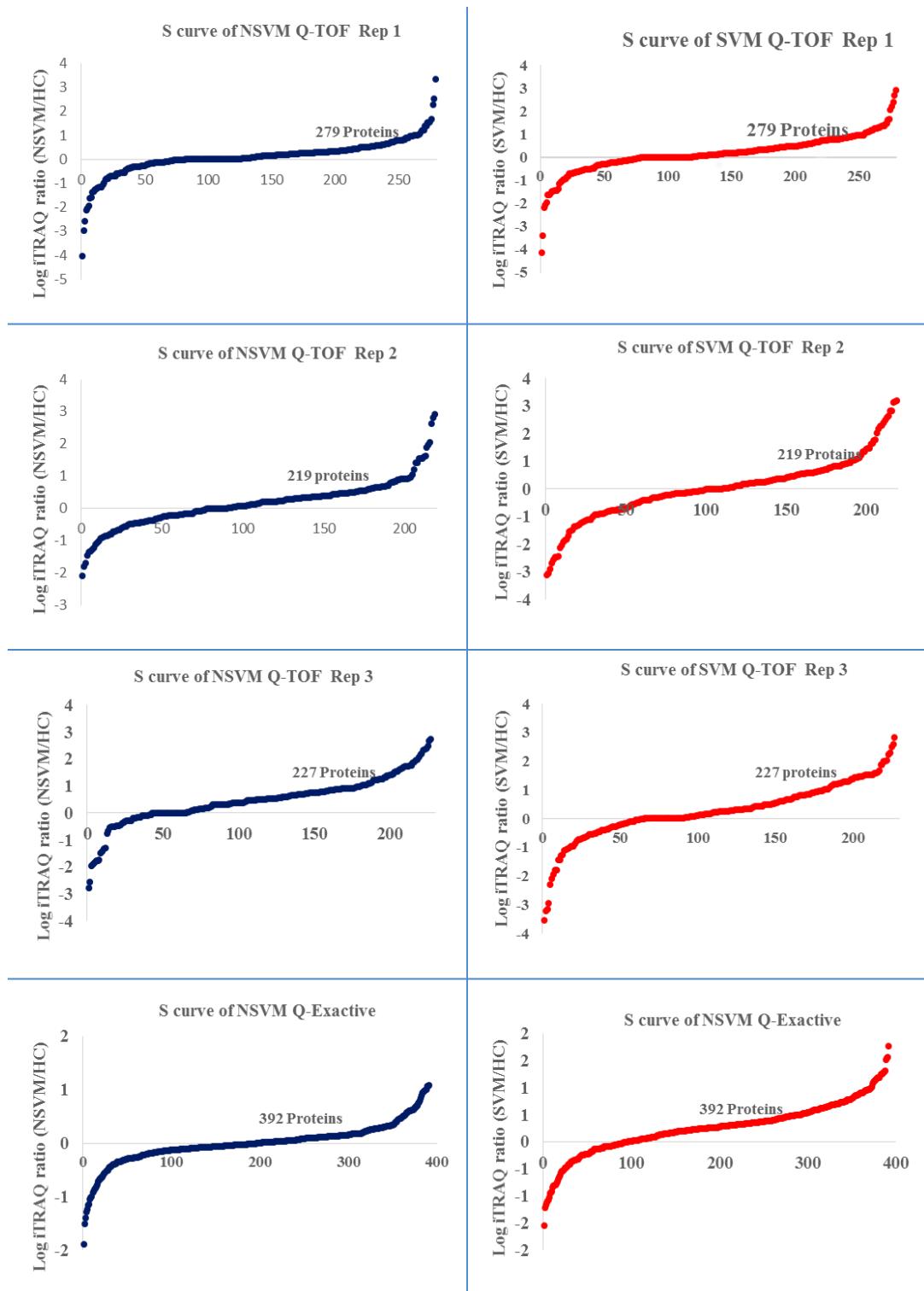
**Figure S3.** Venn diagrams showing the unique and overlapping differentially abundant proteins in NSVM and SVM identified in iTRAQ/DIGE analysis

**Figure S4.** IPA defined networks and pathways associated with the differentially abundant serum proteins in non-severe and severe vivax malaria.

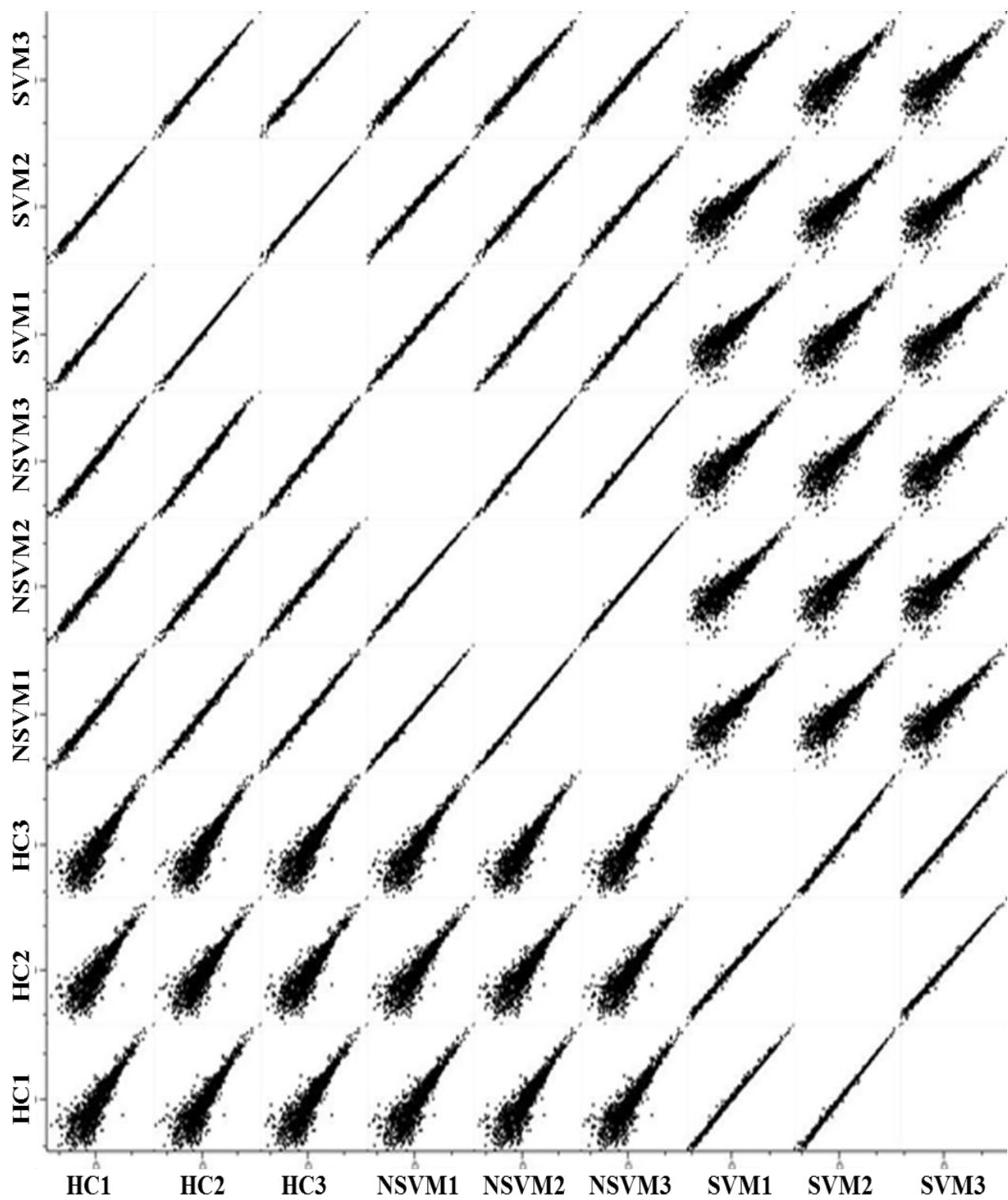
**Figure S5.** ROC curves depicting accuracy of 8 differentially abundant proteins for prediction of malaria and other infectious diseases.



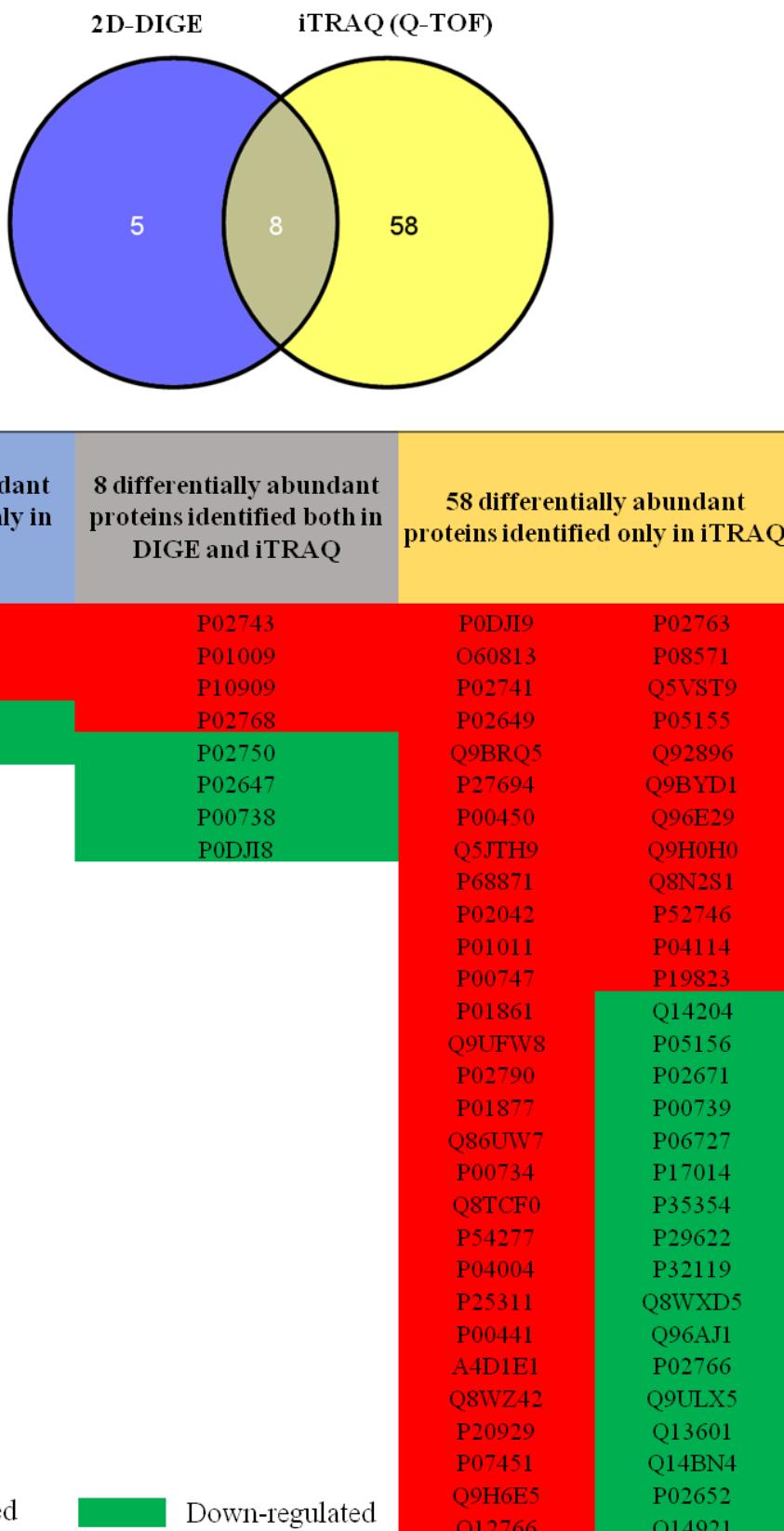
**Figure S1.** Analysis of clinicopathological parameters in healthy community controls (HC), non-severe vivax malaria (NSVM), severe vivax malaria (SVM), dengue fever (DF), and leptospirosis (LEP) patients.



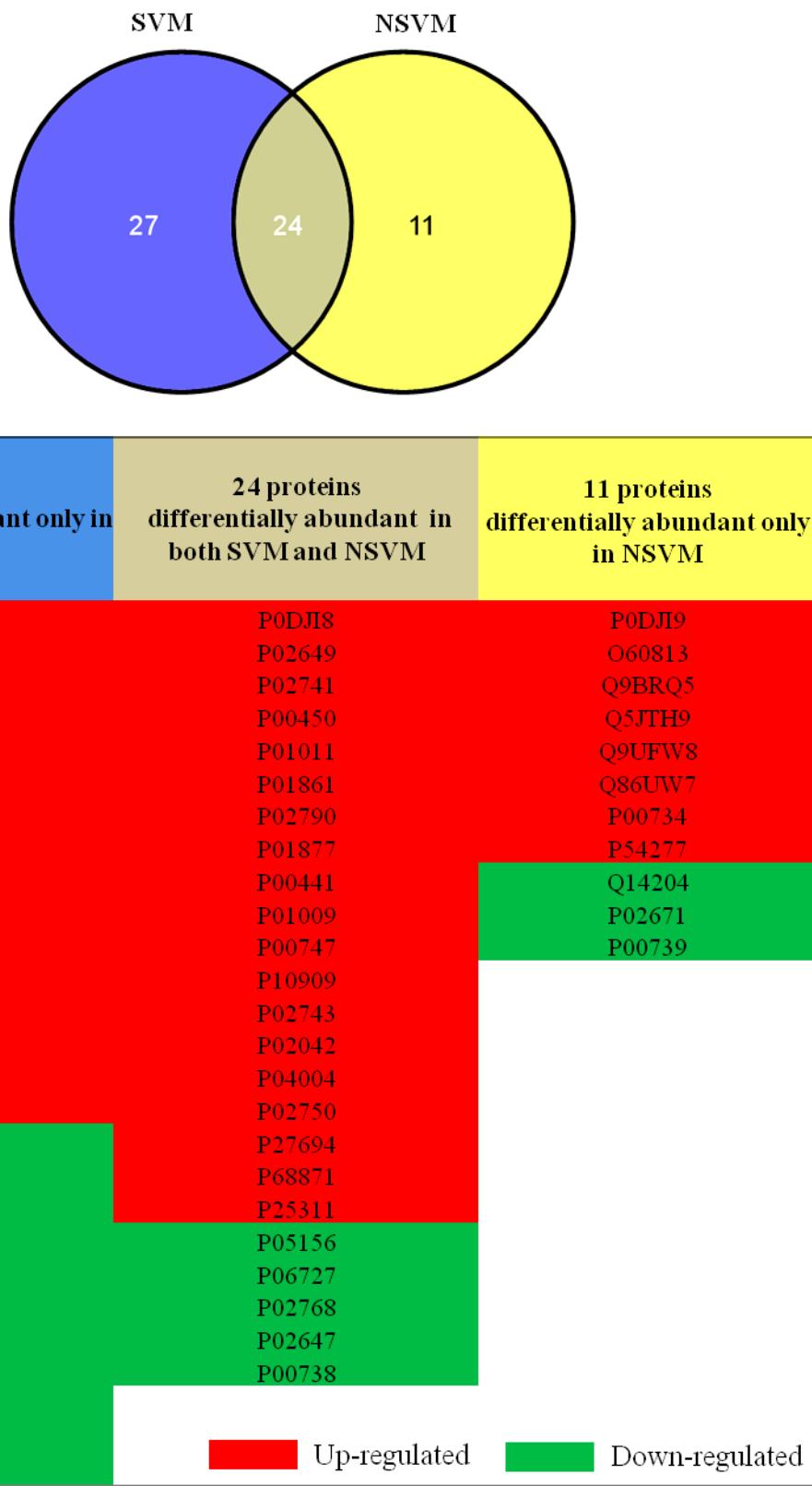
**Figure S2.** (A) Distribution of the differentially abundant proteins in severe and non-severe vivax malaria identified in iTRAQ-based quantitative proteomics analysis (Q-TOF and Q-Exactive)



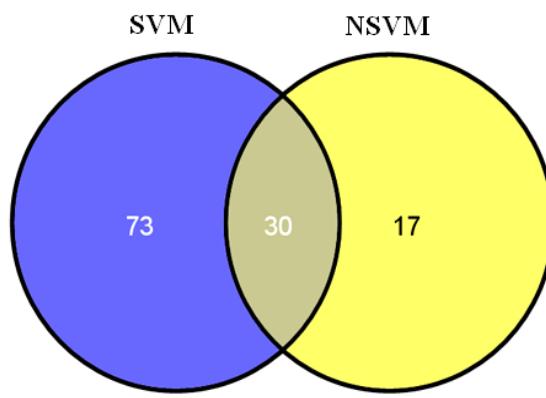
**Figure S2. (B)** Scatter plots exhibiting correlations among the different iTRAQ data sets (analyzed by using Q-TOF).



**Figure S3. (A)** Venn diagram showing the unique and overlapped differentially abundant proteins in vivax malaria identified in 2D-DIGE and iTRAQ (Q-TOF) analysis ( $p \leq 0.05$ ).



**Figure S3. (B)** Venn diagram showing the unique and common differentially abundant proteins in NSVM and SVM identified in iTRAQ analysis by Q-TOF (Fold-change  $\geq 1.2$ ;  $p \leq 0.05$ ).

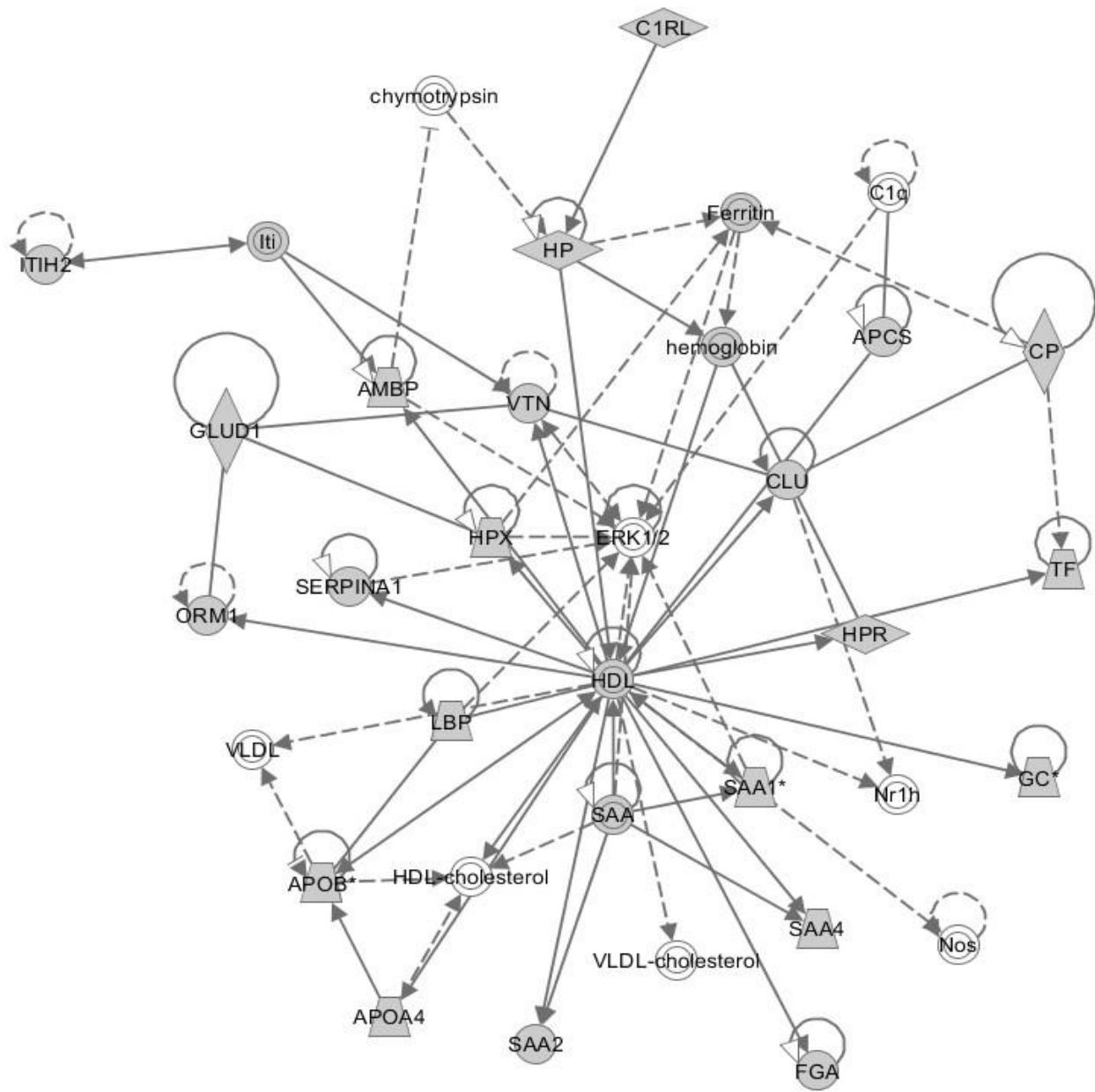


73 proteins differentially abundant only in SVM	30 proteins differentially abundant in both SVM and NSVM	17 proteins differentially abundant only in NSVM
P02679	Q8TCF0	C9J6N2
Q8N5F4	E9PKC6	U3PXP0
S4R394	S6BGF9	P0DJL9
P02675	A2JIN0	D3DQX7
Q96JD0	Q5NV91	Q4TZM4
G3V2B9	A2JIN5	B2R5G8
Q5TEH8	Q5NV75	P0DJ18
H0YE54	P02750	Q4G0R1
Q9UL83	D3DPF9	I1VZV6
A8K3E4	P01011	P02790
Q5FWF9	Q9UL82	Q86YQ1
A2MYD2	Q5TBN3	P00450
Q5NV62	Q6GMX6	P01009
A2MYC8	A2IPI6	P02649
A2JA19	H0YCJ8	P02741
P04220	A2KBC6	P00747
Q6ZW64	P02042	P02743
P00918	P02763	D6RF35
Q5NV92	O95229	P04004
Q9H3B5	F5GX85	B2R9V7
B2RCH7	P02747	C0JYY2
Q9UL85	A2MYD0	P00739
H2B4M3	S6BGD6	P01023
A0NA61	Q96SA9	P06727
B7Z570	A2J1M2	P02647
P01625	P02652	A8K5J7
Q3ZCV0	D6RJG4	P00738
P01814	Q5VY30	H0Y7N4
P00915	K7EQB3	Q05BW3
P01591	A4LAA3	P35527
P01717	Q8N8X9	
Q9P084	B3KXB6	
Q9UL88	C9J8U1	
P06889	P02768	
P01008	Q76B58	
H0YCE5		
D3DPI9		
P06311		

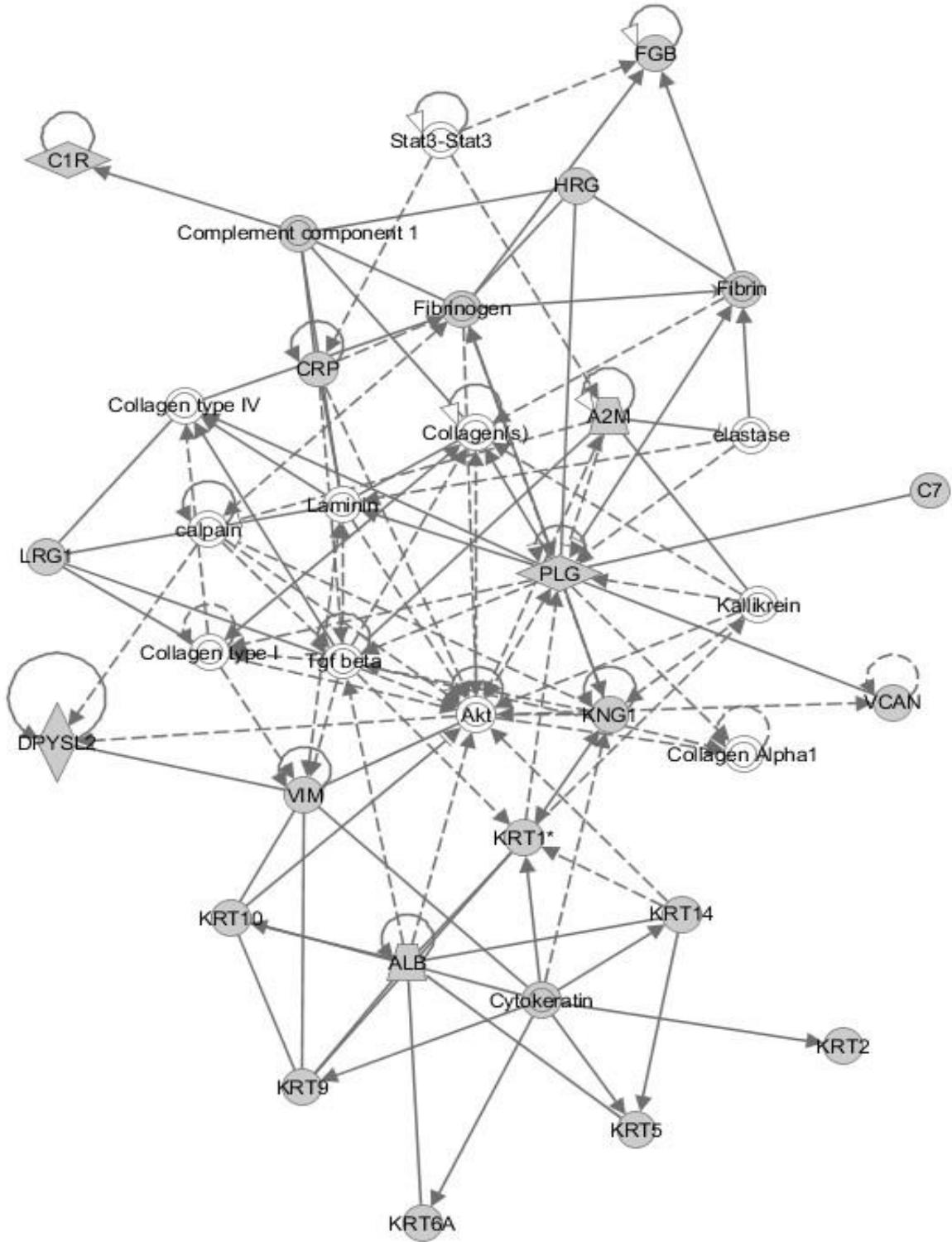
■ Up-regulated      ■ Down-regulated

**Figure S3. (C)** Venn diagram showing the unique and common differentially abundant proteins in NSVM and SVM identified in iTRAQ analysis by Q-Exactive (Fold-change  $\geq 1.5$ ).

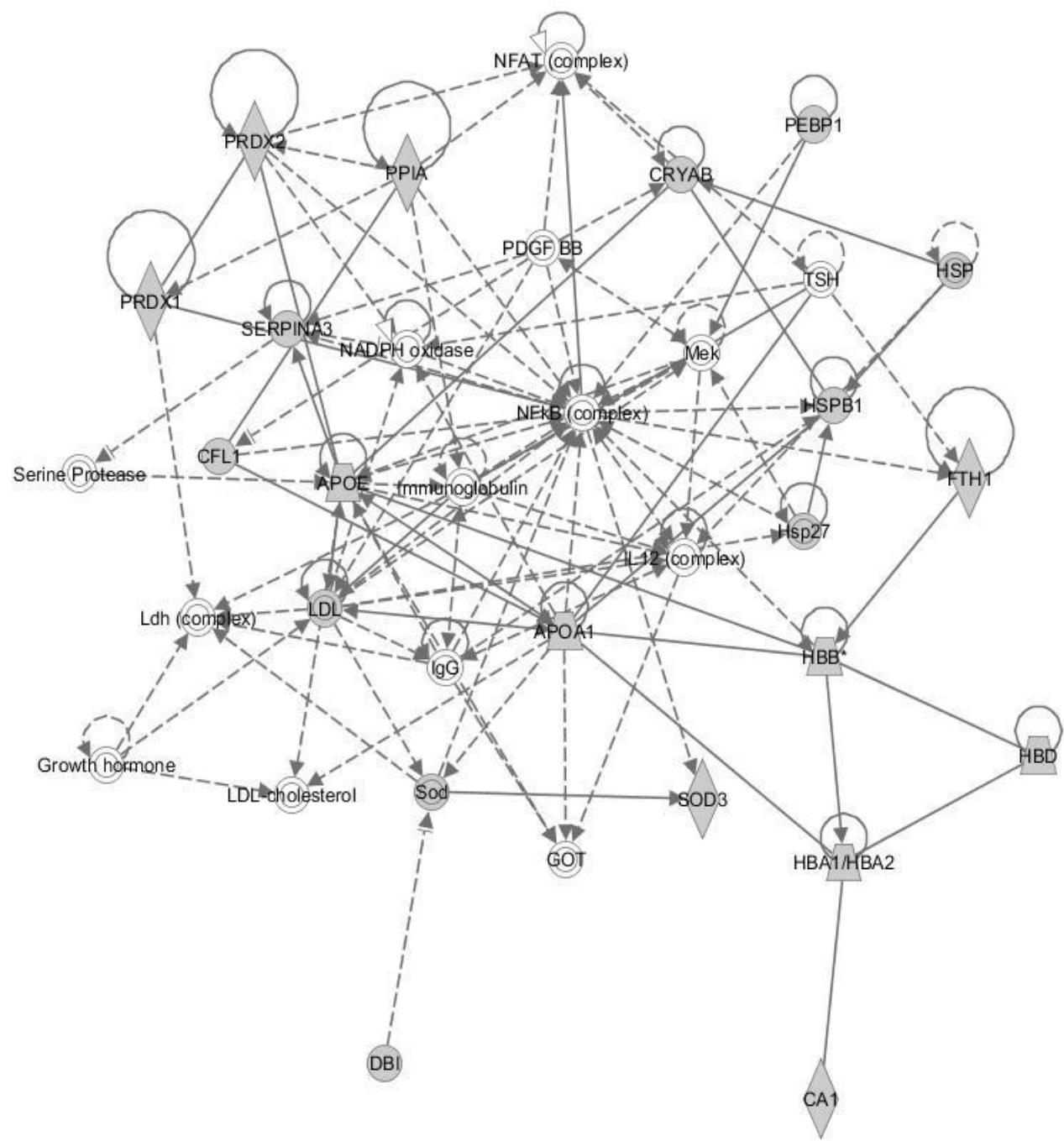
## Interaction networks defined by Ingenuity Pathways Analysis in non-severe *P. vivax* infection



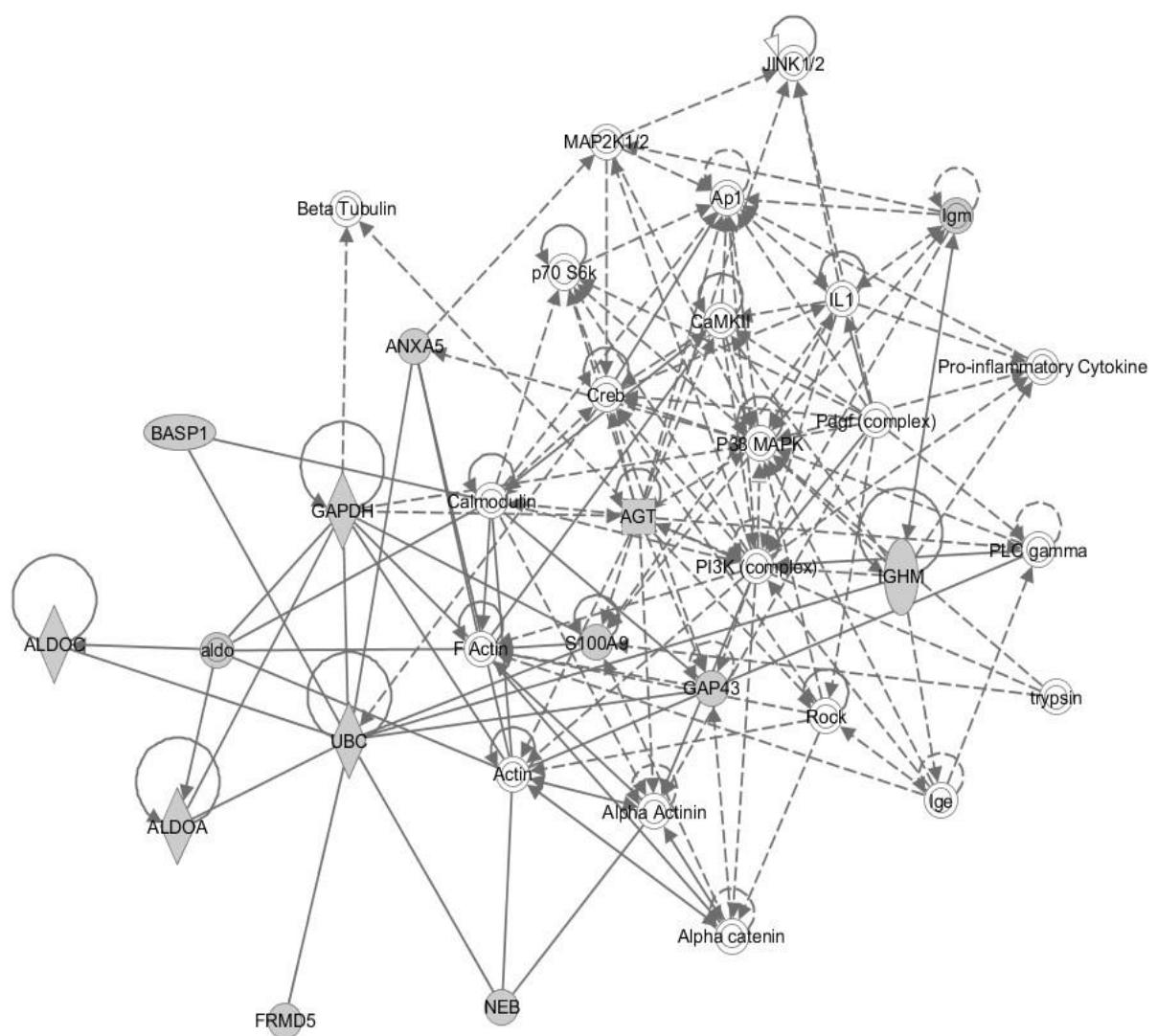
**Cell-To-Cell Signaling and Interaction, Tissue Development, Cancer**



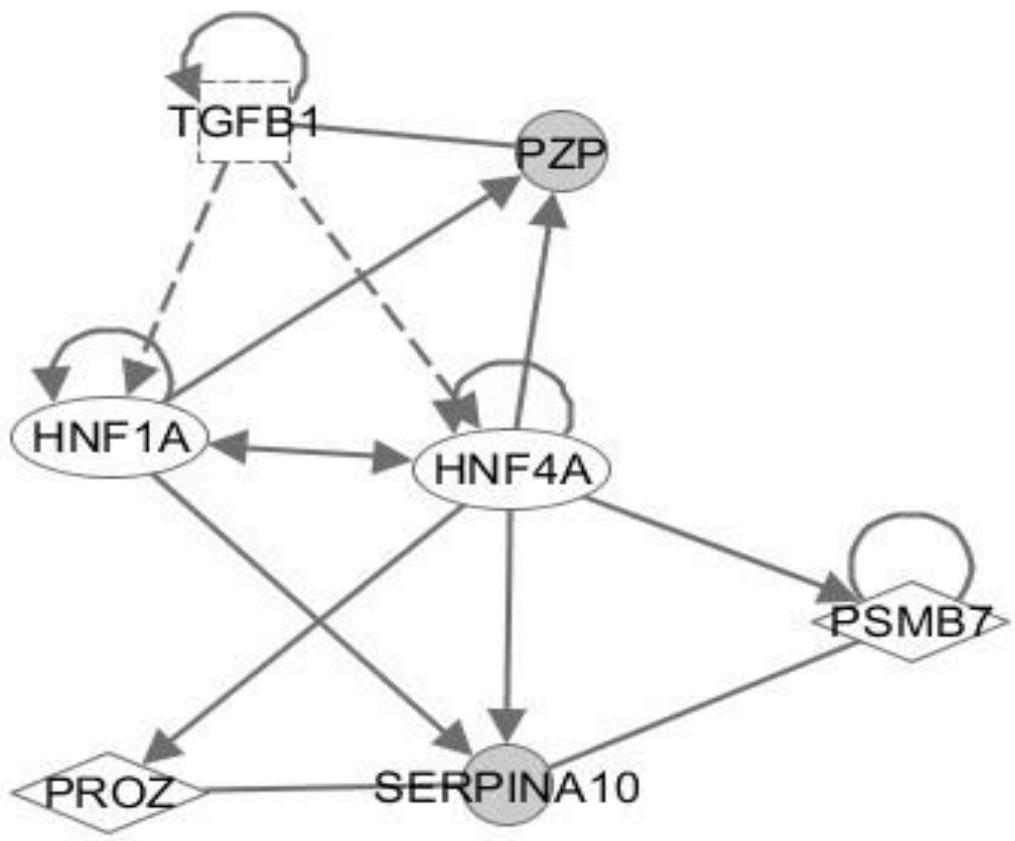
## **Humoral Immune Response, Inflammatory Response, Inflammatory Disease**



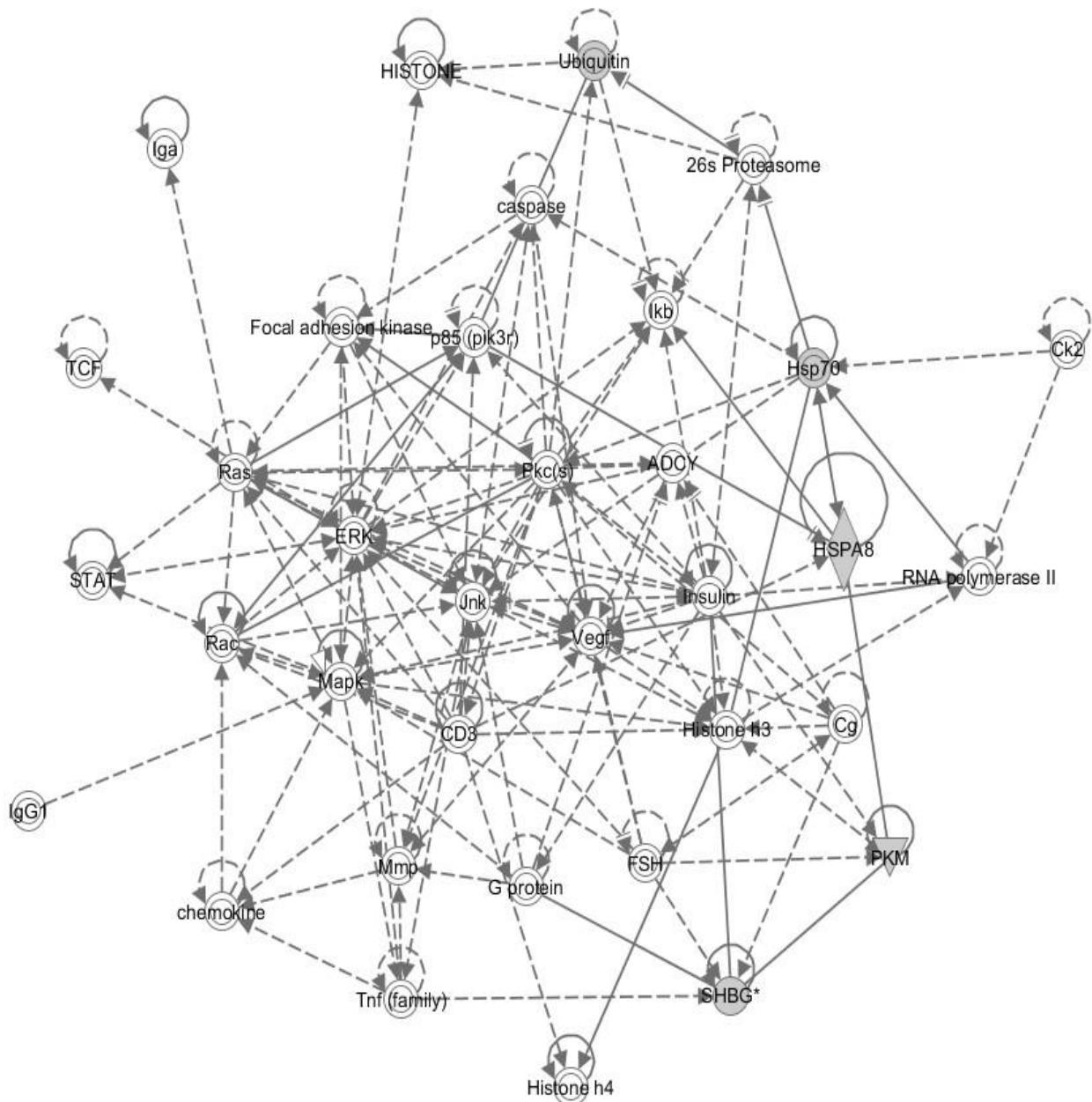
**Free Radical Scavenging, Hematological System Development and Function, Hematopoiesis**



Carbohydrate Metabolism, Small Molecule Biochemistry, Cell Morphology



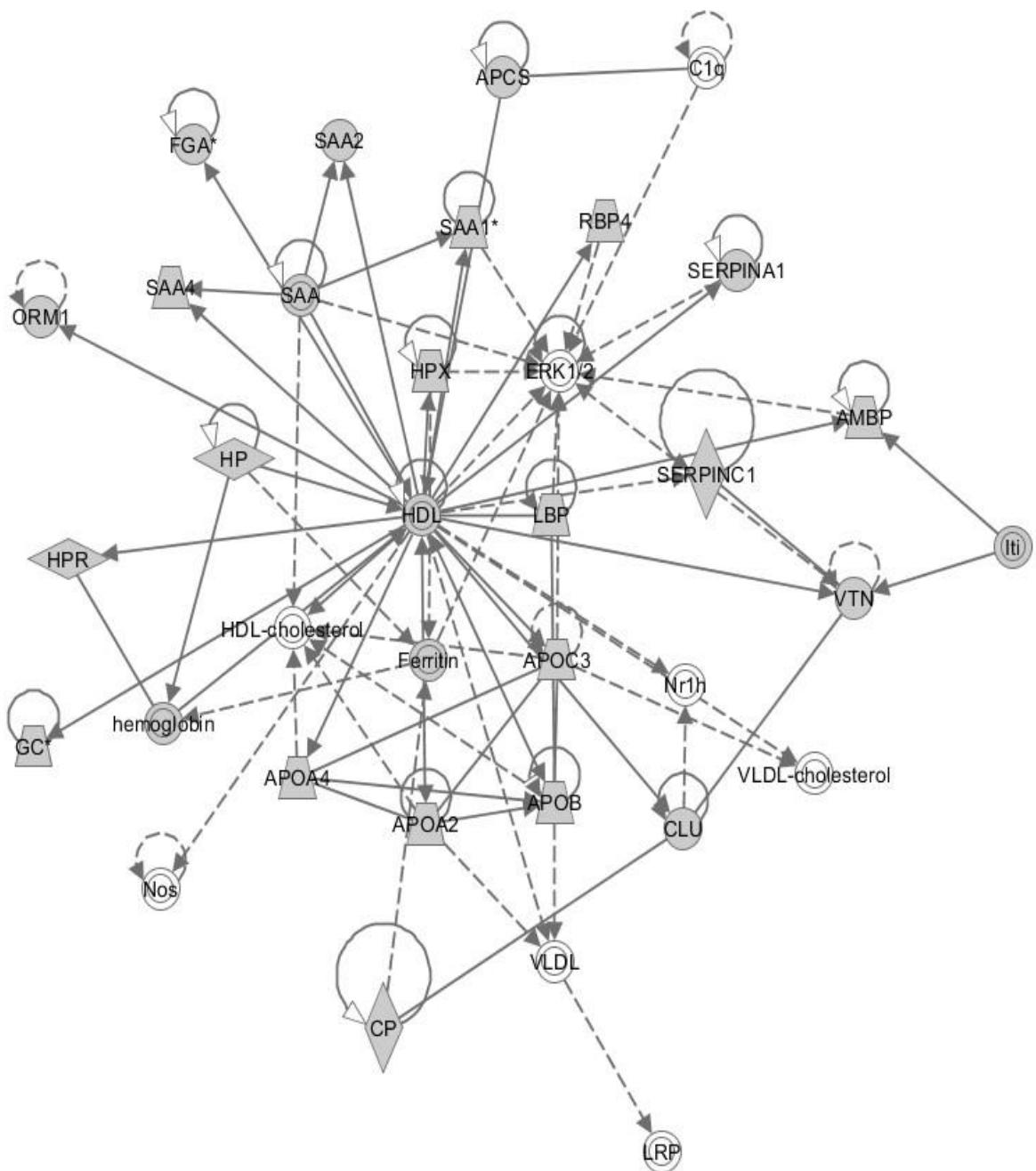
**Cellular Development, Digestive System Development and Function, Hepatic System Development and Function**



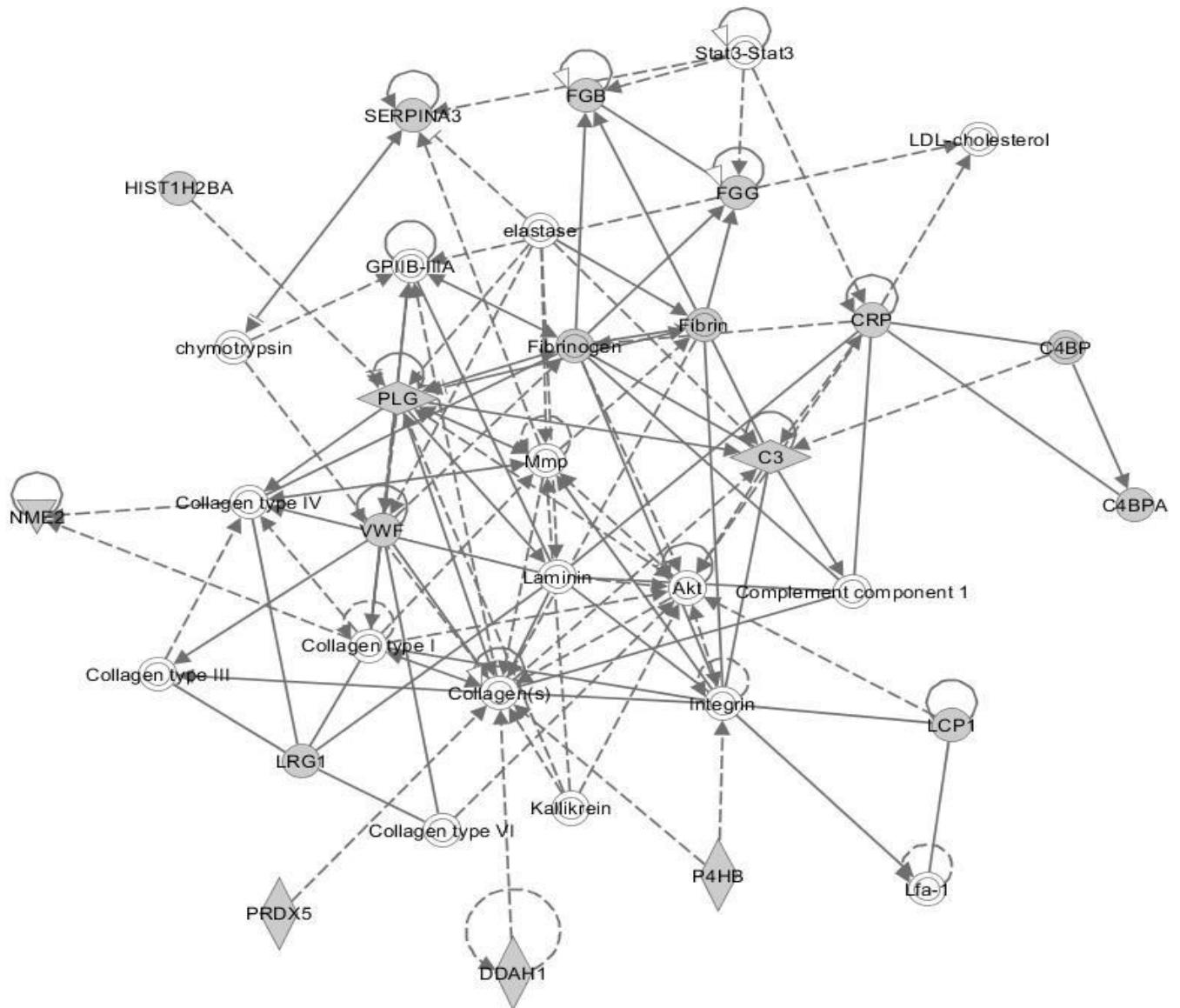
#### Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry

**Figure S4. A.** IPA defined networks associated with the differentially abundant serum proteins in non-severe vivax malaria

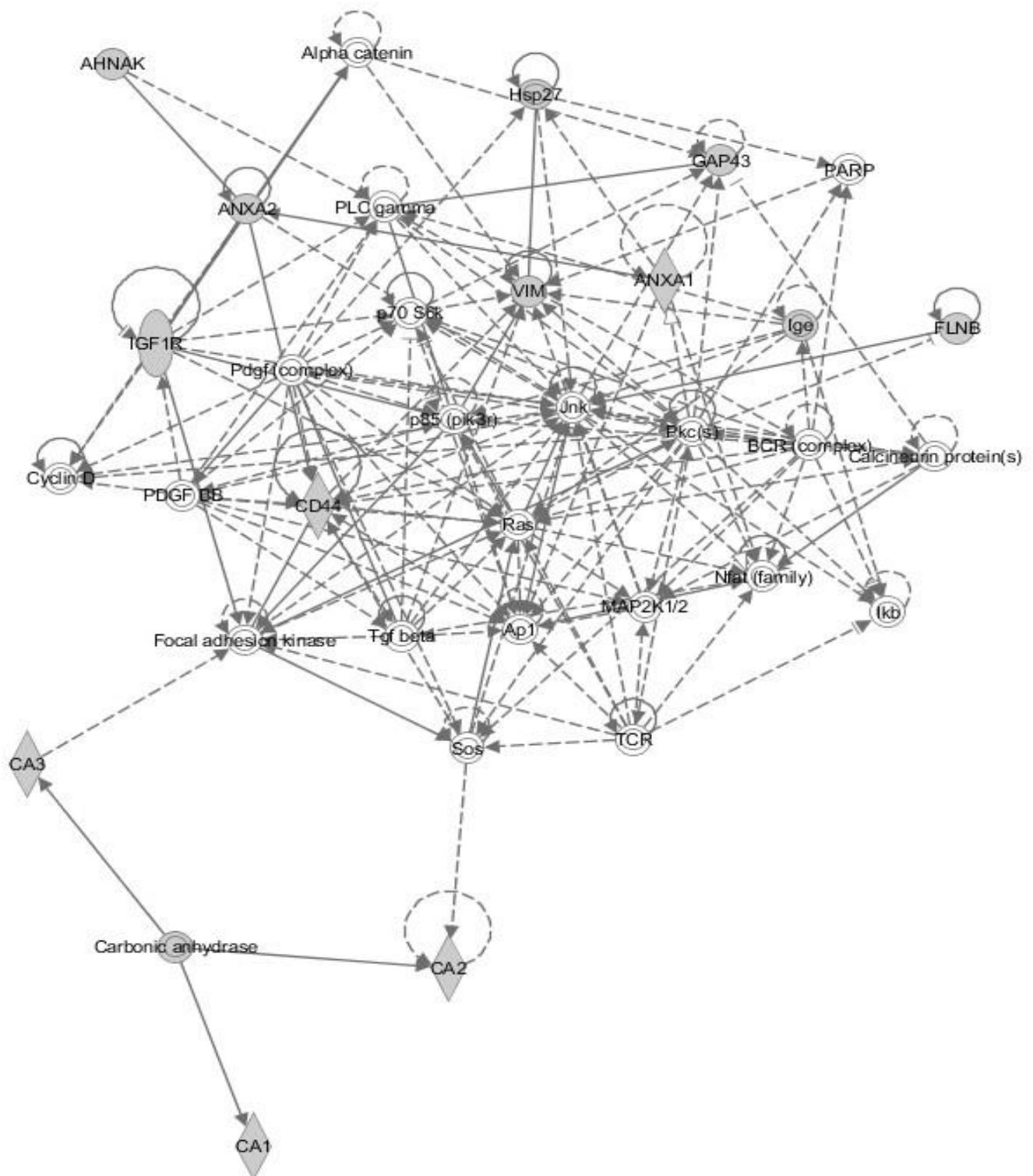
## Interaction networks defined by Ingenuity Pathways Analysis in severe vivax malaria



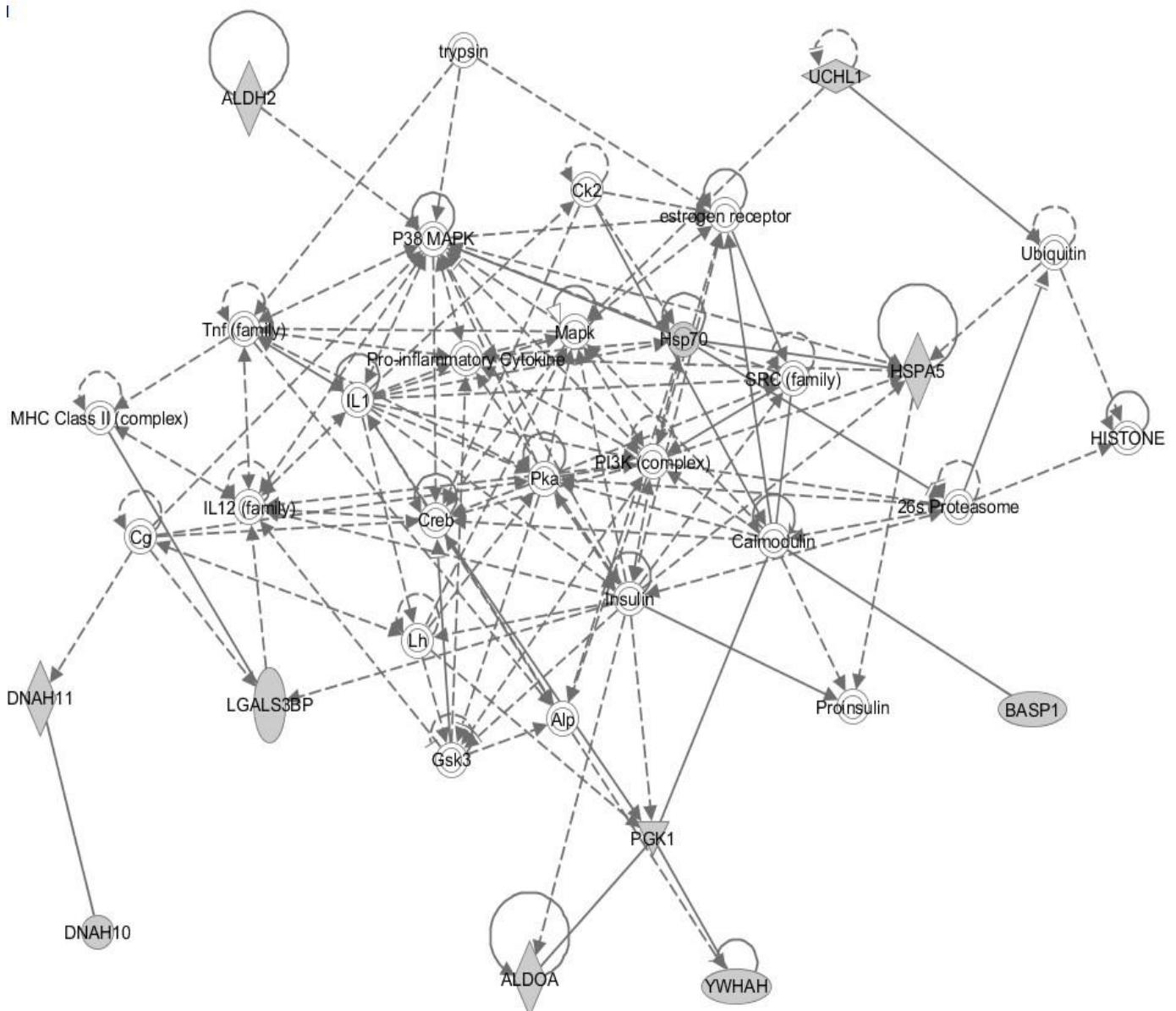
Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry



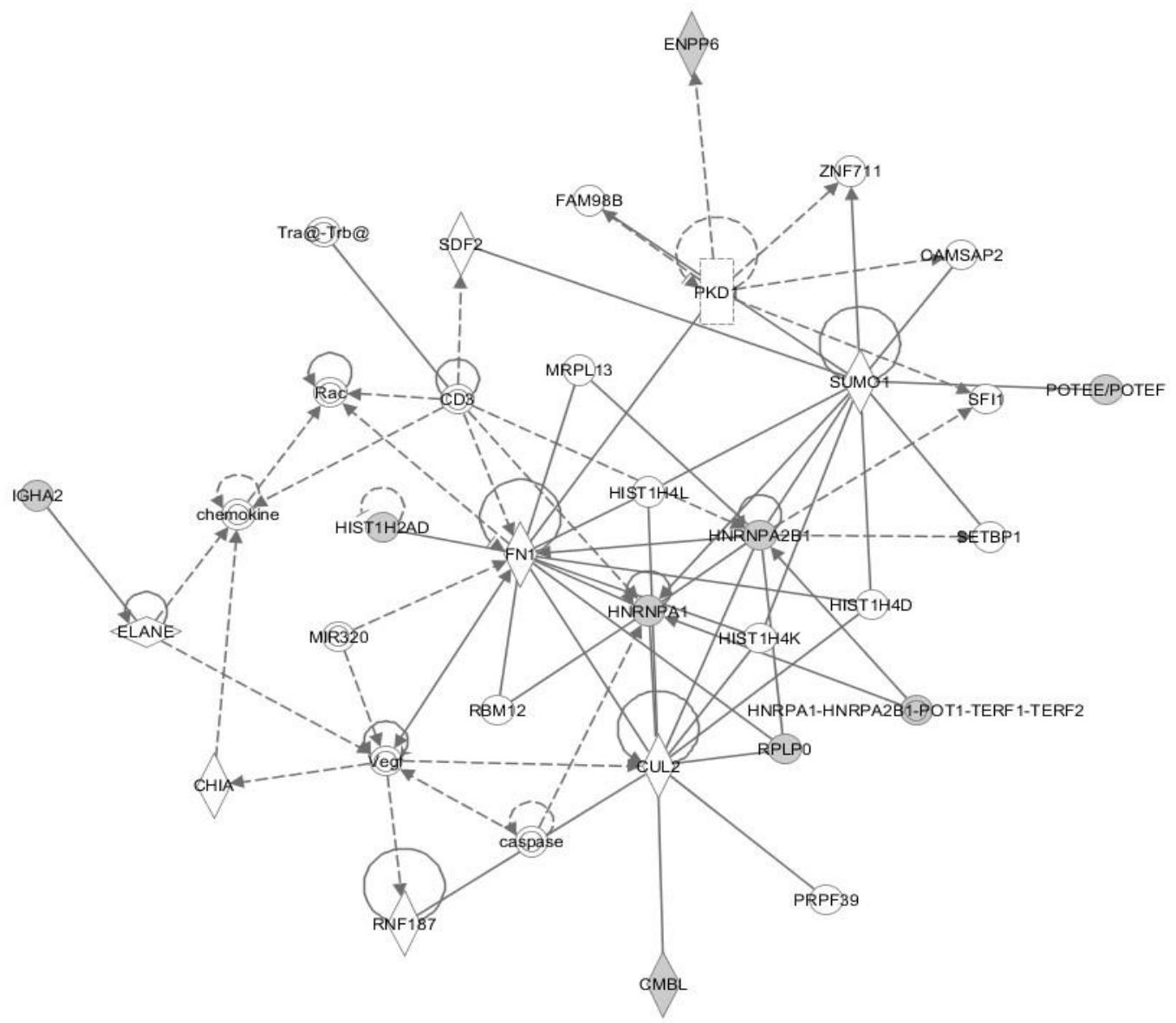
Hematological System Development and Function, Tissue Development, Inflammatory Response



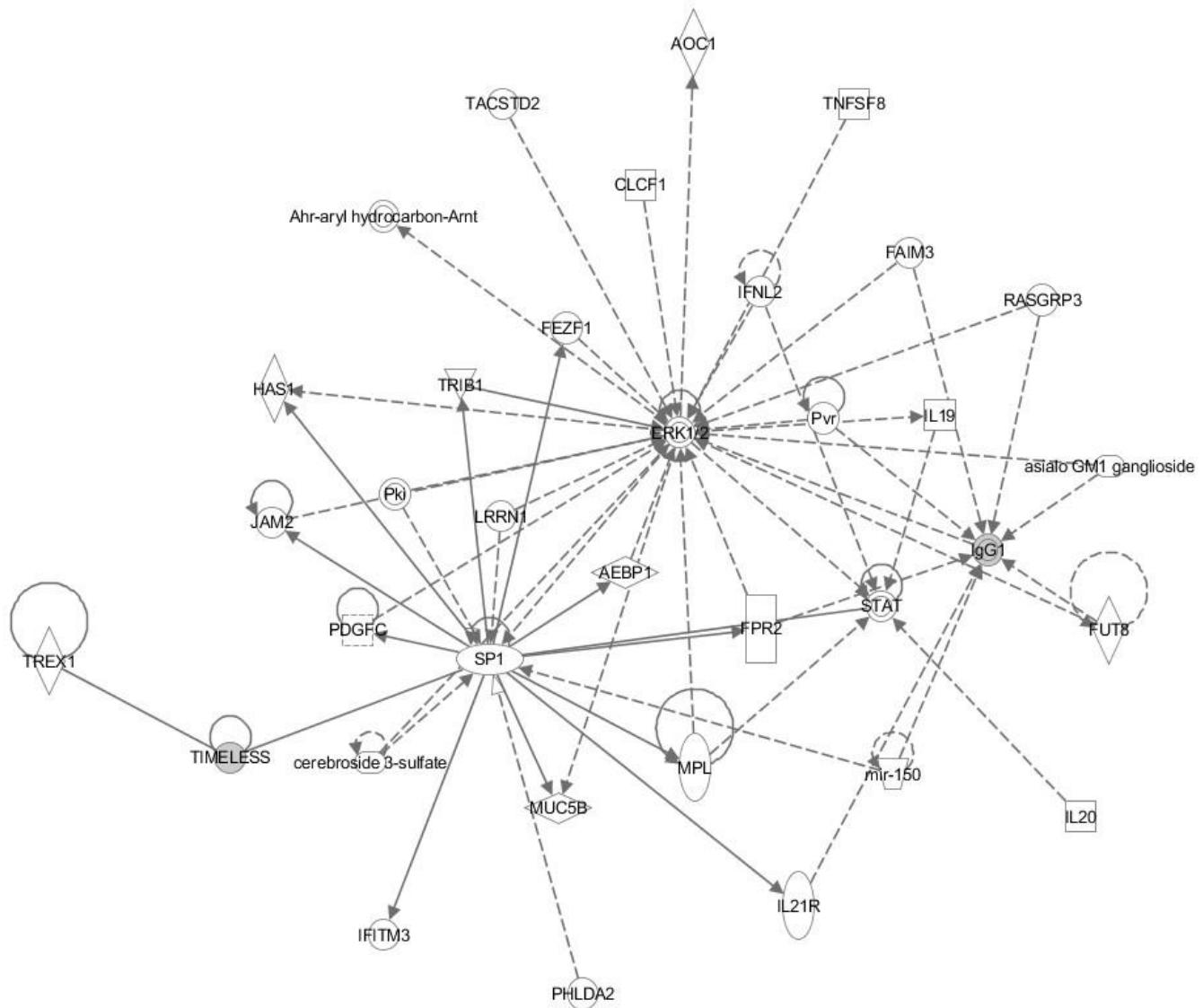
Inflammatory Disease, Inflammatory Response, Ophthalmic Disease



Hematological Disease, Immunological Disease, Inflammatory Disease

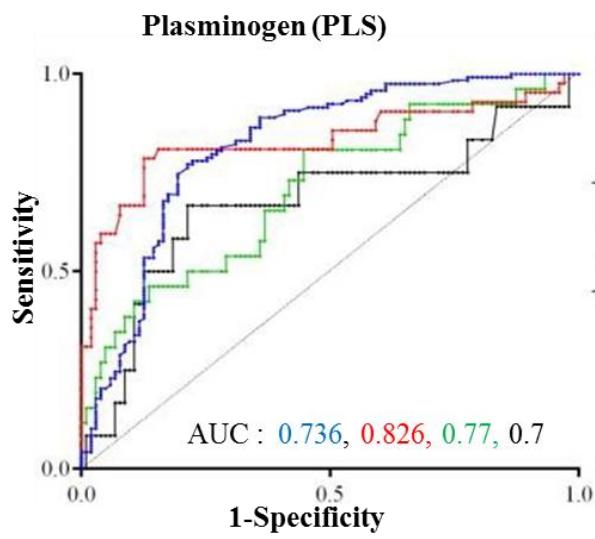
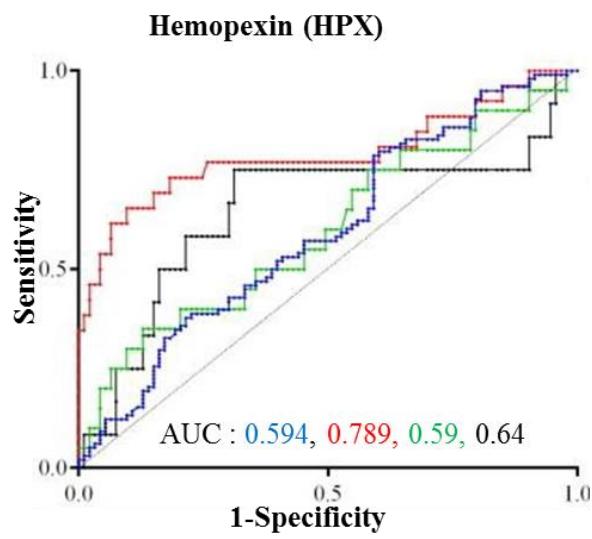
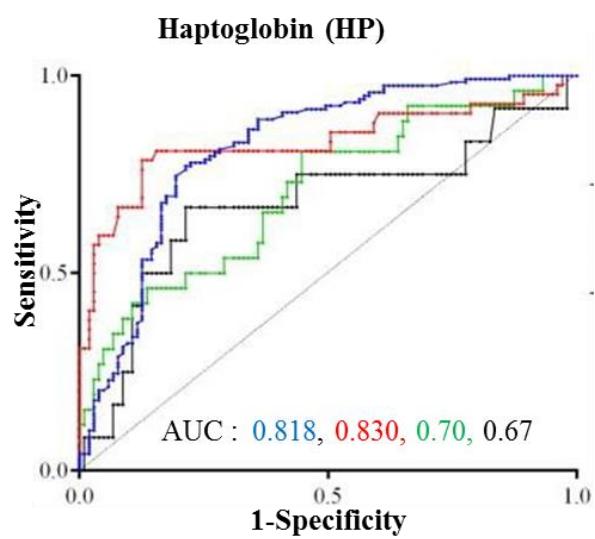
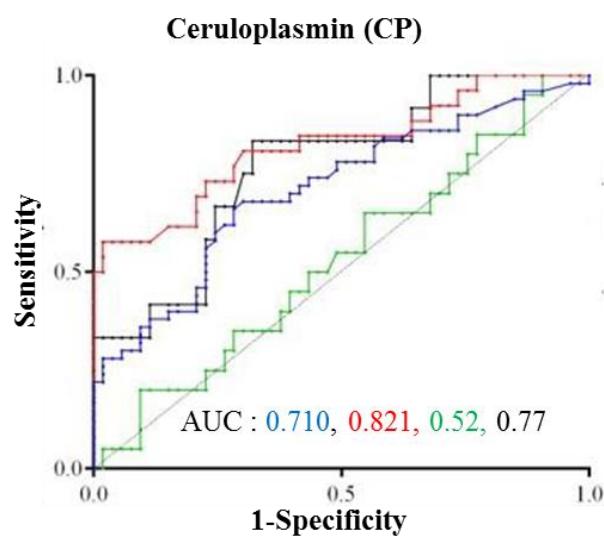
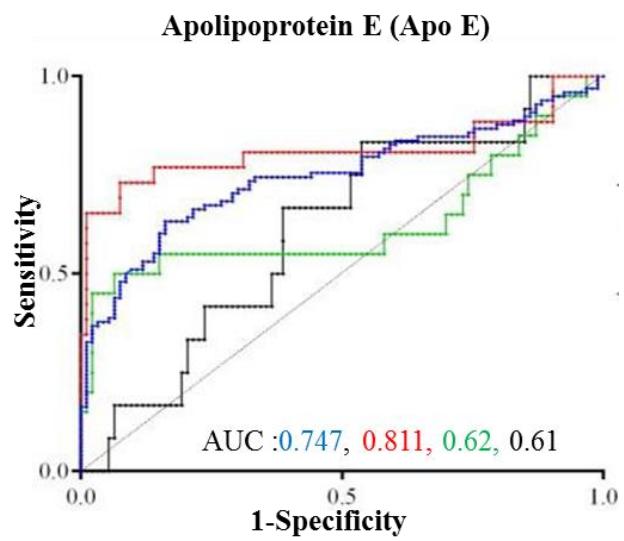
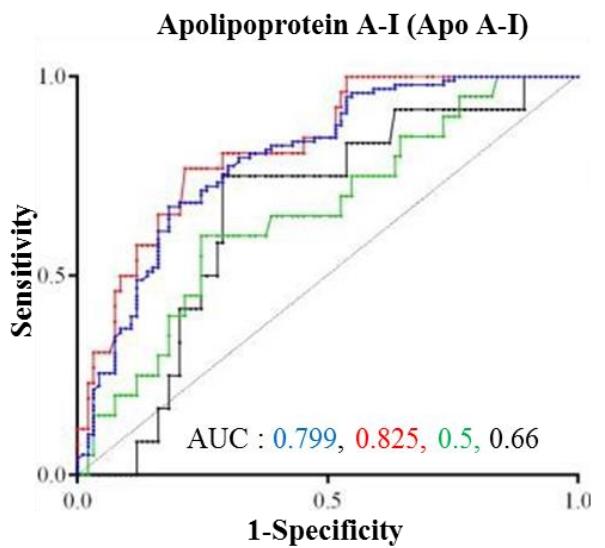


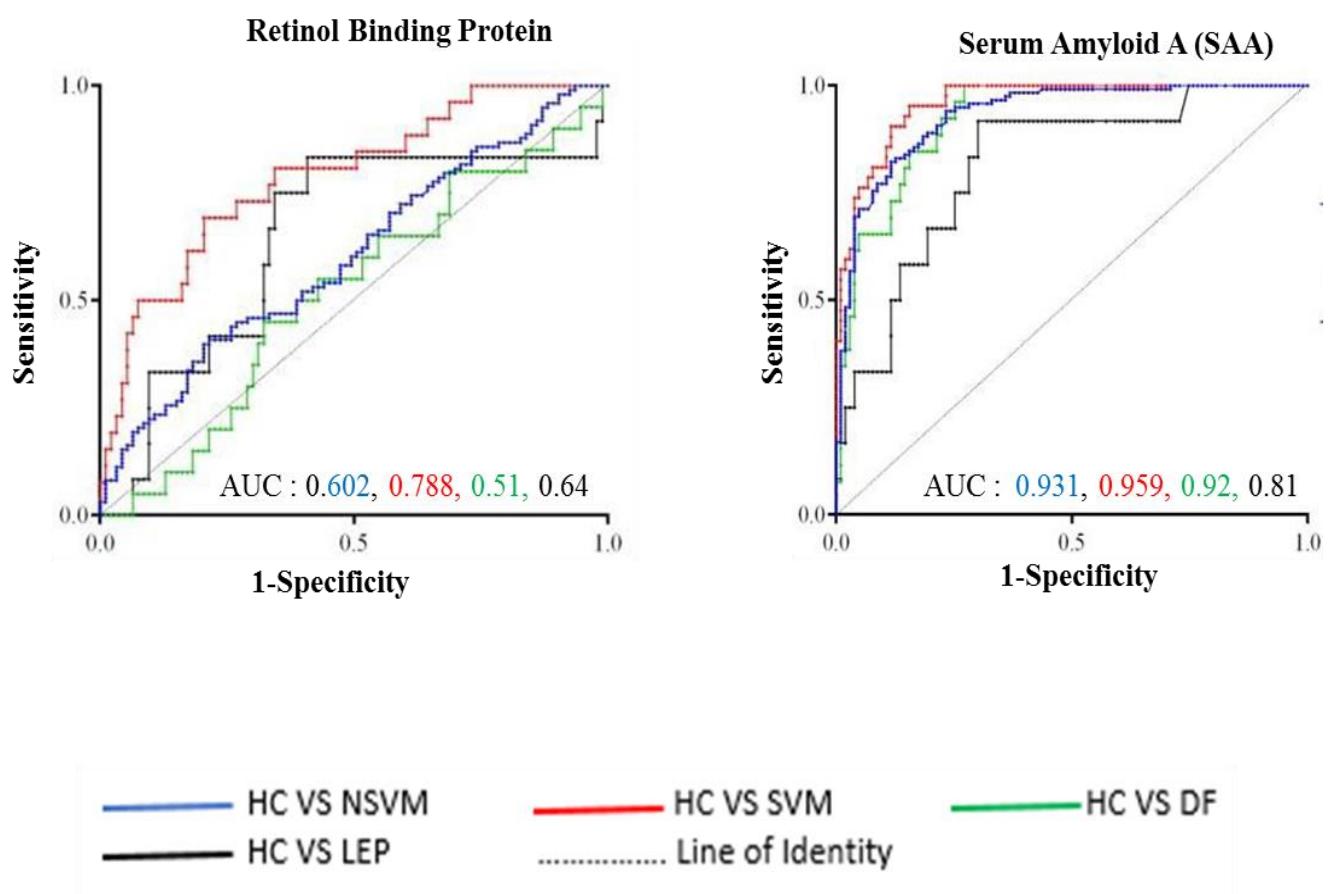
Connective Tissue Disorders, Developmental Disorder, Hereditary Disorder



### Humoral Immune Response, Protein Synthesis, Cellular Growth and Proliferation

**Figure S4. B.** IPA defined networks associated with the differentially abundant serum proteins in severe vivax malaria





**Figure S5.** ROC curves depicting accuracy of 8 differentially abundant proteins for prediction of vivax malaria and other infectious diseases.