

## Supplementary Data

# Modeling interaction between non-structural protein 2 of Chikungunya Virus and various protein factors of innate pathway

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**Table S1:** Analysis of stereochemical stability of nsP2 of CHIKV genotypes and human innate immune proteins

<b>Accession number</b>	<b>Virus/Host Proteins</b>	<b>Template</b>	<b>Sequence Identity</b>	<b>ERRAT score</b>
MF774616.1	Asian genotype nsP2	6jim.1	100%	93.13
ANH22444.1	WA genotype nsP2	6jim.1	98.06%	93.13
AID69222.1	ECSA genotype nsP2	6jim.1	99.57	93.13
O95786.2	RIG-I	5f9f.1.E	100	85.18
BAE79738.1	IPS-1	3j6j.1.A	98.97	81.00
NP_663777.1	TRAF3	1flk.1.A	100	85.12
NP_004611.1	TRAF6	1ca9.2.B	27.57	81.00
AAO74498.1	TRIF	2m1w.1.A	99.38	70.34

**Table S2:** Analysis of pyDock complexes of nsP2 of CHIKV genotypes and human innate immune proteins

*Note:* arbitrary unit (a.u), Kilocalories per mole (kcal/mole)

<b>Genotype</b>	<b>Van der Waals energy (Kcal/mol)</b>	<b>Electrostatic energy (Kcal/mol)</b>	<b>Desolvation energy (Kcal/mol)</b>	<b>Total pyDock energy</b>
Asian-IPS1	0.983	-30.081	-4.734	-34.717
WA-IPS1	0.983	-30.081	-4.734	-34.717
ECSA-IPS1	47.589	-15.429	-24.207	-34.877
Asian -RIGI	6.875	-19.971	-15.708	-34.991
WA-RIGI	6.875	-19.971	-15.708	-34.991
ECSA-RIG1	20.824	-9.785	-31.511	-39.213
Asian-TRIF	11.551	-42.530	1.061	-40.314
WA-TRIF	11.551	-42.530	1.061	-40.314
ECSA-TRIF	78.736	-27.185	-19.541	-38.853
Asian-TRAF3	11.293	-7.648	-34.216	-40.735
WA-TRAF3	11.293	-7.648	-34.216	-40.735
ECSA-TRAF3	23.158	-8.924	-34.719	-41.327
Asian-TRAF6	30.811	-21.340	-7.620	-25.880
WA-TRAF6	30.811	-21.340	-7.620	-25.880
ECSA-TRAF6	15.681	-19.133	-8.464	-26.029

**Table. S3:** Bonding nature of interactive residues among the bimolecular complex of nsP2 of CHIKV genotypes and RIG-I.

Disulfide bond					
ECSA CHIKV nsP2	RIG-I	WA CHIKV nsP2	RIG-I	Asian CHIKV nsP2	RIG-I
Lys 481	Glu 83	Lys 481	Glu 83	Asp 546	Lys 105
Asp 550	Arg 75	Asp 550	Arg 75		
Hydrogen bond					
Asp 663	Ser 52	Arg 660	Tyr 106	Asn 476	Leu 19
Tyr 666	Pro 43	Arg 660	Ser 107	Thr 675	Glu 114
Arg 660	Leu 54	Arg 660	Ser 55	Thr 675	Glu 114
Arg 660	Pro 39	Arg 660	Lys 105	Thr 675	Ser 79
Asn 667	Glu 22	Leu 657	Ser 110	Ala 674	Glu 114
Phe 471	Glu 83	Lys 474	Glu 83	Ala 545	Ser 40
Lys 481	Glu 83	Lys 481	Glu 83	Asp 546	Val 109
Lys 481	His 82	Asp 663	Ser 52	Asp 546	Lys 105
Glu 669	Ser 110	Tyr 666	Pro 43	Arg 552	Ser 55
Ala 545	Arg 75	Thr 675	Leu 19	Arg 552	Ser 55
His 548	Arg 75	His 548	Asn 77	Arg 660	Ser 3
Asp 550	Arg 75	Asn 547	Glu 15	Arg 660	Pro 4
Asp 550	Arg 75	Asp 550	Arg 75	Ala 662	Arg 75
Asp 546	Tyr 74	Ala 545	Arg 75	Thr 665	Arg 75
Asp 546	Gln 6			Tyr 666	Asn77
Asp 547	Glu 15				

**Note:** Bonding interactions were compared, using bimolecular complex data of nsP2 of CHIKV genotypes: East Central South Africa (ECSA), West Africa (WA), and Asian with retinoic acid-inducible gene I (RIG-I). The three letter represents the amino acid name and numbers represents the bond position between the virus-host protein chains.

**Table. S4:** Bonding nature of interactive residues among the bimolecular complex of nsP2 of CHIKV genotypes and IPS-1.

<b>Disulfide bond</b>					
<b>ECSA CHIKV nsP2</b>	<b>IPS-1</b>	<b>WA CHIKV nsP2</b>	<b>IPS-1</b>	<b>Asian CHIKV nsP2</b>	<b>IPS-1</b>
Arg 660	Asp 38	Asp 509	Lys 7	Asp 546	Arg 37
Asp 663	Arg 41	Asp 509	Lys 10	Arg 552	Asp 40
Asp 550	Arg 98	Asp 663	Arg 64	Asp 550	Arg 64
		Asp 546	Arg 52	Lys 481	Asp 53
<b>Hydrogen bond</b>					
Arg 660	Asp 38	His 548	Asn 15	Asp 546	Arg 37
Arg 660	Thr 35	His 548	Arg 14	Asp 546	Arg 64
Val 659	Arg 64	Ala 475	Arg 14	Ala 545	Arg 64
Thr 665	Arg 64	Asn 476	Lys 10	Ala 545	Arg 64
Ala 662	Arg 64	Glu 508	Lys 7	Asp 550	Arg 64
Tyr 666	Asn 60	Asp 509	Lys 7	Asn 547	Gln 63
Thr 675	Asp 6	Asp 509	Lys 7	Lys 481	Asp 53
Thr 675	Asp 6	Asp 509	Lys 10	Asn 476	Asp 6
Ala 674	Asp 6	Asp 509	Lys 10	Asp 509	Tyr 9
Leu 670	Met 1	Asn 667	Asp 6	Ala 475	Tyr 9
Asn 547	Met 1	Thr 675	His 57	Ala 475	Asn 60
Asp 546	Arg 98	Tyr 666	Arg 41	Gly 661	Arg 98
Lys 481	Thr 99	Tyr 666	Thr 61	Ala 662	Arg 98
Asp 550	Arg 98	Thr 665	Asn 60	Val 659	Arg 98
Asp 550	Arg 98	Thr 665	Arg 64	Arg 660	Ser 94
Arg 552	Arg 98	Ala 662	Arg 64	Asn 667	Met 1
His 548	Arg 98	Asp 546	Arg 52		
His 548	Thr 99	Asn 547	Cys 13		

**Note:** Bonding interactions were compared, using bimolecular complex data of nsP2 of CHIKV genotypes: East Central South Africa (ECSA), West Africa (WA), and Asian with interferon-beta promoter stimulator 1 (IPS-1). The three letter represents the amino acid name and numbers represents the bond position between the virus-host protein chains.

**Table. S5:** Bonding nature of interactive residues among the bimolecular complex of nsP2 of CHIKV genotypes and TRAF3.

<b>Disulfide bond</b>					
<b>ECSA CHIKV nsP2</b>	<b>TRAF 3</b>	<b>WA CHIKV nsP2</b>	<b>TRAF 3</b>	<b>Asian CHIKV nsP2</b>	<b>TRAF 3</b>
Asp 550	Arg 405	Glu 625	Lys 523	Asp 711	Arg 398
Lys 481	Asp 403	Glu 625	Arg 479	Asp 711	Arg 405
		Asp 663	Arg 405	Arg 714	Asp403
		Arg 660	Asp 401	Asp 531	Arg 387
		Asp 546	Arg 387		
<b>Hydrogen bond</b>					
Arg 660	Leu 381	Arg 623	Thr 525	Tyr 666	Tyr 449
Arg 660	Leu 380	Leu 646	Glu 481	Thr 675	Leu 409
Val 659	Arg 387	Glu 625	Lys 523	Met 707	Arg 398
Asn 551	Tyr 414	Glu 625	Arg 479	Asp 711	Arg 398
Pro 656	Arg 387	Gly 661	Arg 405	Asp 711	Arg 398
Tyr 543	Glu 481	Asn 643	Arg 479	Asp 711	Arg 405
Asp 550	Arg 405	Asp 663	Arg 405	Gln 706	Arg 398
His 548	Met 402	Gly 658	Asp 401	Gln 706	Arg 398
Ala 545	Arg 405	Arg 660	Asp 401	Asn 547	Asp 701
Lys 481	Asp 403	Arg 660	Asp 401	Tyr 544	Asp 401
Asp 546	Arg 398	Asn 476	Gln 390	Arg 714	Asp 403
Asn 547	Arg 398	Asn 547	Arg 387	Arg 714	Asp 403
				Arg 736	Met 391
				Asp 531	Arg 387
				Leu 530	Arg 387
				Phe 535	Gln 390
				Lys 556	Gln 390
				Met 557	Gln 390
				Arg 570	Gln 373

**Note:** Bonding interactions were compared, using bimolecular complex data of nsP2 of CHIKV genotypes: East Central South Africa (ECSA), West Africa (WA), and Asian with tumor necrosis factor receptor-associated factor 3 (TRAF3). The three letter represents the amino acid name and numbers represents the bond position between the virus-host protein chains.

**Table. S6:** Bonding nature of interactive residues among the bimolecular complex of nsP2 of CHIKV genotypes and TRAF6.

Disulfide bond					
ECSA CHIKV nsP2	TRAF6	WA CHIKV nsP2	TRAF6	Asian CHIKV nsP2	TRAF6
Arg 660	Asp 339	Lys 481	Glu 345	Glu 625	Arg 461
Arg 660	Glu 343	Asp 550	Lys 340	Arg 660	Asp 339
Glu 669	Arg 332	Arg 552	Glu 417	Arg 660	Glu 343
Glu 625	Arg 461	Arg 552	Glu 343	Glu 669	Arg 332
His 548	Glu 321			Asp 546	Lys 319
Lys 481	Glu 321			His 548	Glu 321
Asp 546	Lys 319			Lys 481	Glu 321
Hydrogen bond					
Arg 660	Asp 339	Lys 481	Glu 345	Glu 625	Arg 461
Arg 660	Asp 339	Ala 545	Lys 340	Arg 660	Asp 339
Arg 660	Glu 343	His 548	Lys 340	Arg 660	Asp 339
Asn 643	Glu 417	His 548	Lys 340	Arg 660	Glu 343
Gly 658	Thr 336	Asp 550	Lys 340	Ala 645	Ser 420
Ala 662	Lys 340	Arg 552	Tyr 381	Tyr 664	Lys 340
Asp 663	Lys 340	Arg 552	Glu 343	Thr 665	Lys 340
Thr 665	Lys 340	Arg 660	Leu 316	Asp 663	Lys 340
Glu 669	Arg 332	Ile 659	Lys 319	Gly 658	Thr 336
Glu 669	Arg 332	Thr 665	Lys 319	Tyr 666	Thr 333
Asn 667	Glu 329	Pro 656	Gln 323	Glu 669	Arg 332
Glu 625	Arg 461	Ala 662	Lys 319	Glu 669	Arg 332
Lys 481	Glu 321			Asp 550	Thr 317
Asp 546	Lys 319			Asp 546	Lys 319
				His 548	Glu 321
				Lys 481	Glu 321

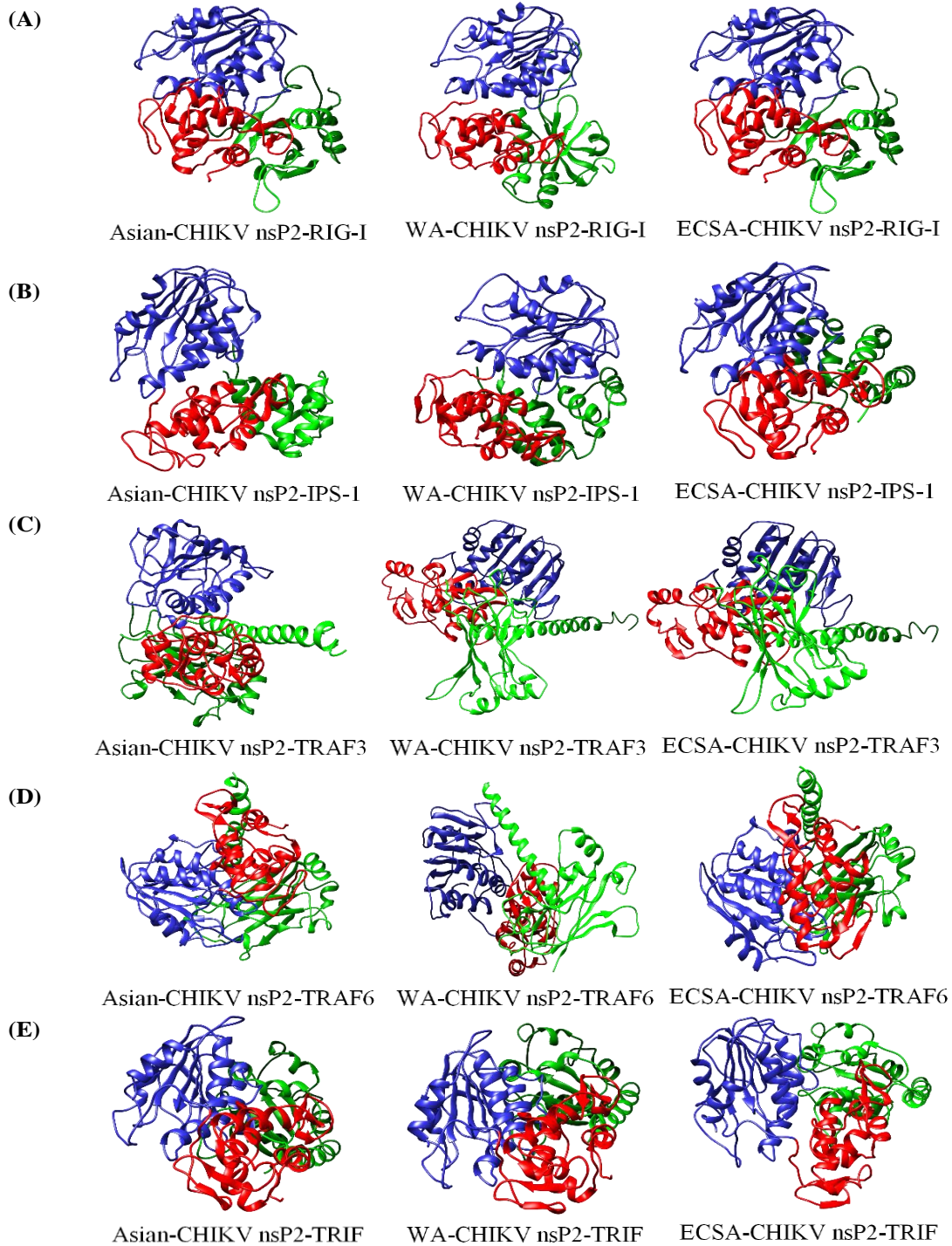
**Note:** Bonding interactions were compared, using bimolecular complex data of nsP2 of CHIKV genotypes: East Central South Africa (ECSA), West Africa (WA), and Asian with tumor necrosis factor receptor-associated factor 6 (TRAF6). The three letter represents the amino acid name and numbers represents the bond position between the virus-host protein chains.

**Table. S7:** Bonding nature of interactive residues among the bimolecular complex of nsP2 of CHIKV genotypes and TRIF.

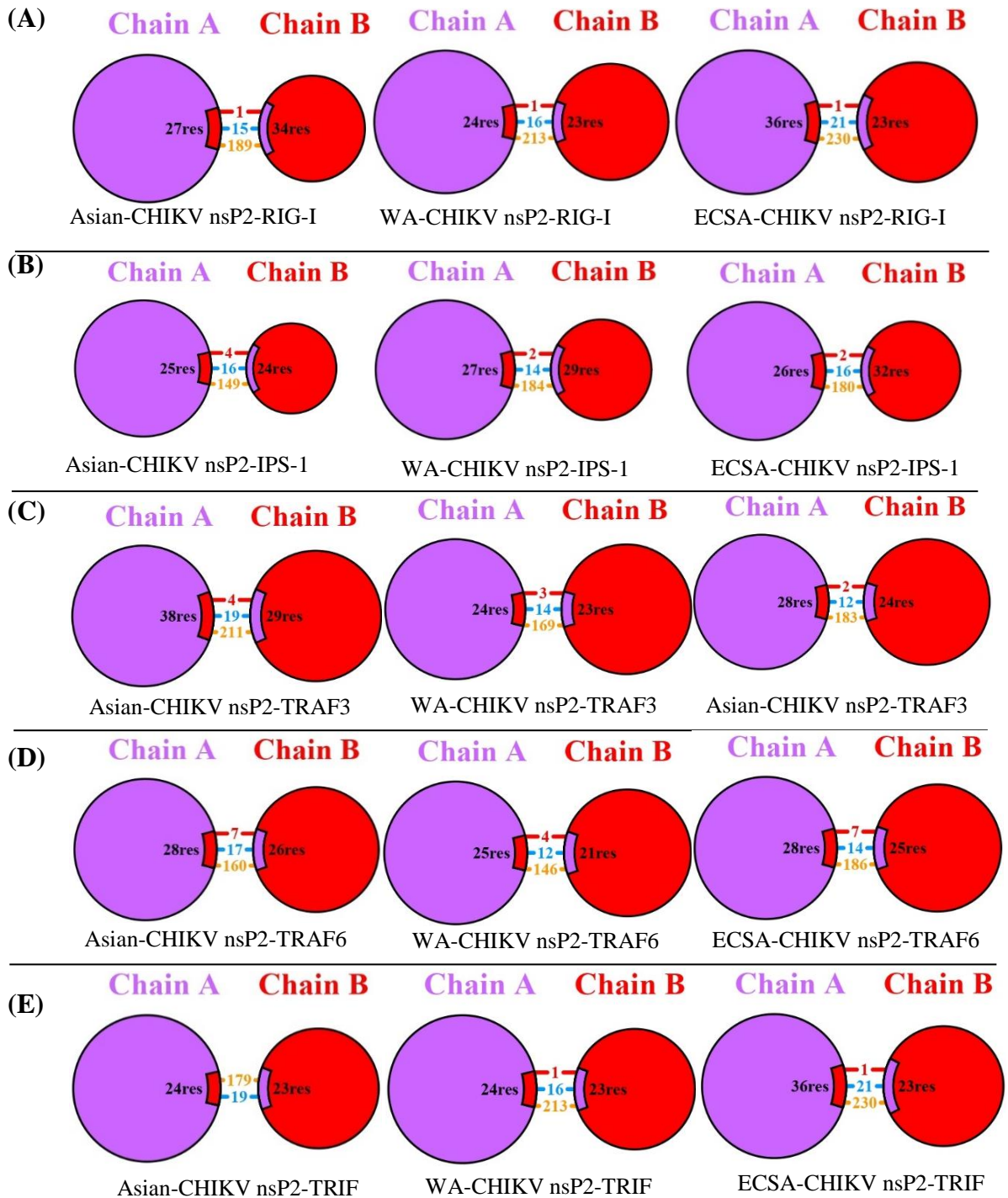
<b>Disulfide bond</b>					
<b>ECSA CHIKV nsP2</b>	<b>TRIF</b>	<b>WA CHIKV nsP2</b>	<b>TRIF</b>	<b>Asian CHIKV nsP2</b>	<b>TRIF</b>
ARG 660	GLU 87	Arg 660	Asp 127		
<b>Hydrogen bond</b>					
Thr 675	Gln 152	Asn 547	Gln 232	Asn 667	Ala 235
Asn 551	Gln 232	Thr 675	Ser 156	Thr 675	Thr 155
Asn 551	Gln 232	Thr 675	Thr 155	Thr 675	Ser 156
His 548	Ile 234	Leu 676	Thr 155	Sys 478	Arg 231
Lys 481	Ala 235	Tyr 679	Phe153	Ala 475	Arg 231
Val 477	Ala 235	Arg 650	Gln 122	Ala 475	Arg 231
Asp 547	Ser156	Arg 650	Cys 149	Arg 660	Pro 116
Asp 547	Asp159	Tyr 664	Asn 150	Arg 660	Gln 120
Asp 546	Ser 156	Tyr 664	Asn 150	Arg 660	Gln 120
Tyr 544	Tyr 154	Asp 663	Gln 123	Arg 660	Mat 115
Glu 508	His 121	Asp 663	Gln 123	Ala 662	Leu 125
Asn 473	Gln 120	Asp 663	Asn 124	Tyr 664	Asn 150
Leu 657	Gln 123	Asp 663	Asn 124	Tyr 664	Asn 150
Asn 667	Gln 123	Gly 658	Arg 119	Asp 663	Asn 124
Asn 667	Asn 150	Arg 660	Pro 116	Asp 663	Asn 124
Asn 476	Asp 126	Arg 660	Asp 127	Asp 663	Gln 123
Arg 660	Glu 87			Tyr 679	Phe 153
Thr 665	Arg 145			Arg 650	Cys 149
Gly 658	Asp 146			Arg 650	Cys 149
Val 659	Asp 146				
Asp 663	Cys 149				

Bonding interactions were compared, using bimolecular complex data of nsP2 of CHIKV genotypes: East Central South Africa (ECSA), West Africa (WA), and Asian with TIR domain-containing adaptor inducing interferon- $\beta$  (TRIF). The three letter represents the amino acid name and numbers represents the bond position between the virus-host protein chains.

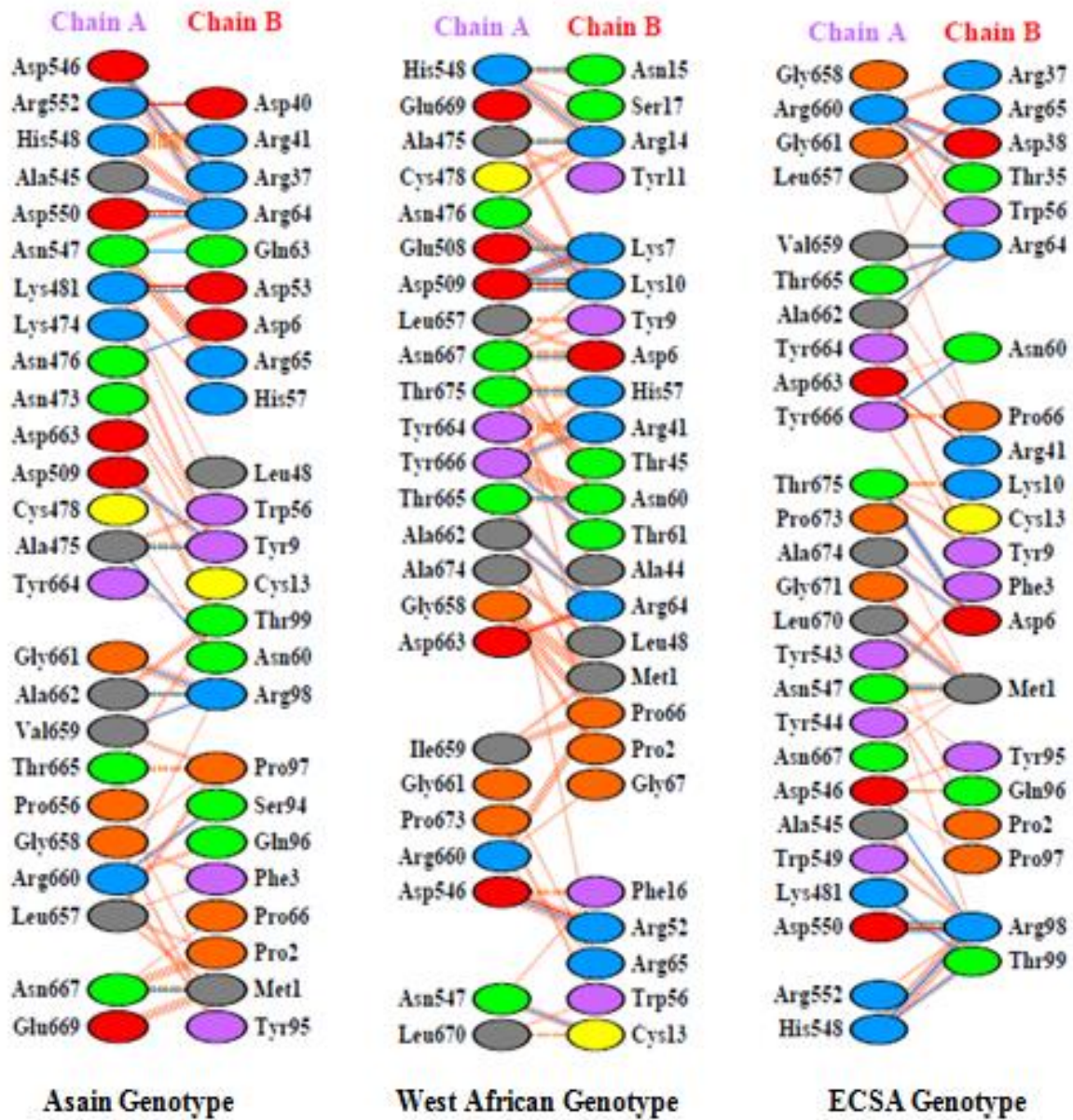




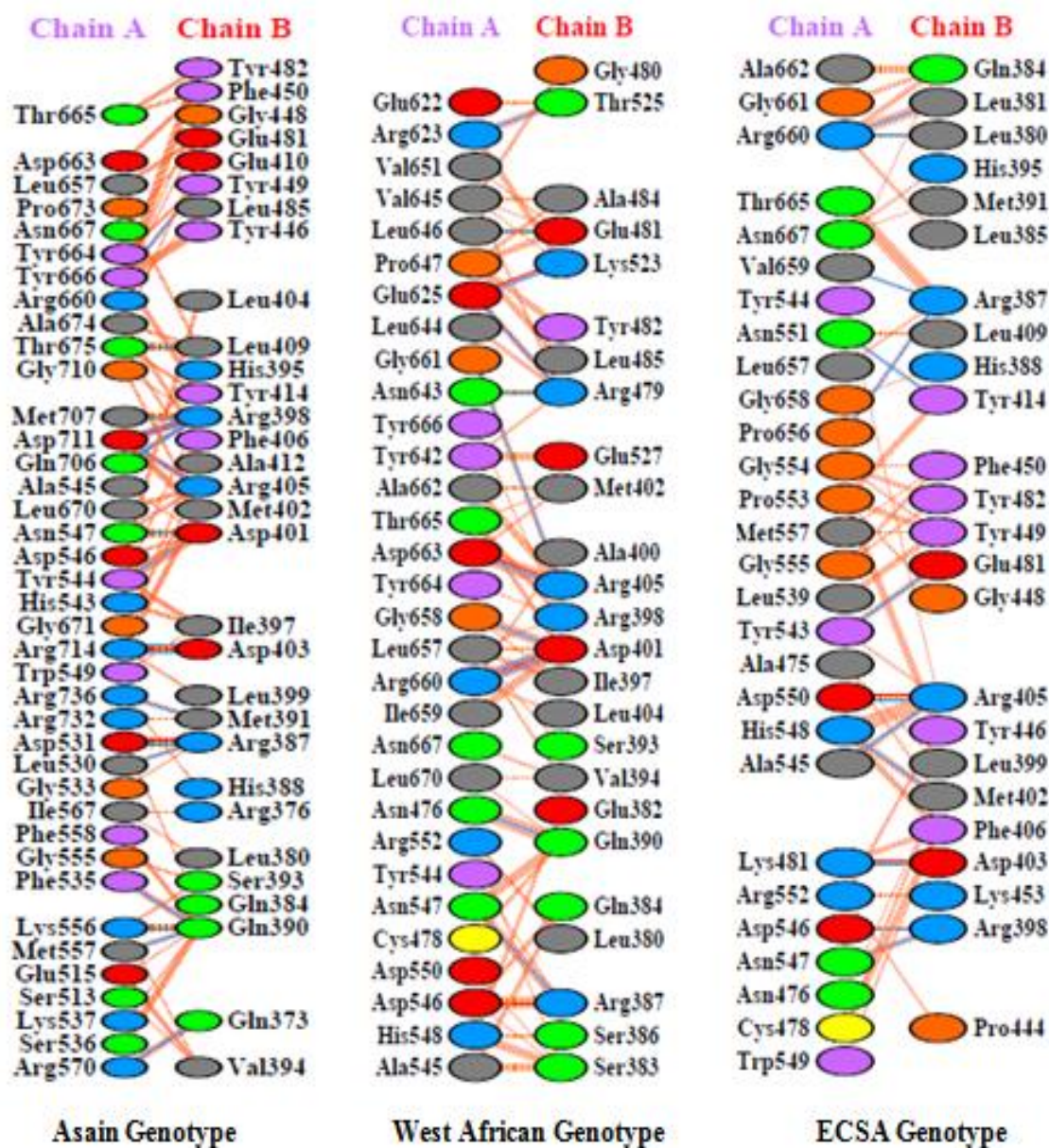
**Fig. S1:** Bimolecular Complex of CHIKV nsP2 and human innate immune pathway proteins. The CHIKV nsP2, protein-like protease domain represented with red color and methyl transferase like domain represented with blue color. The CHIKV nsP2 is involved in viral RNA replication and transcription. The human innate immune pathway proteins represented with green color. (A) Bimolecular complex of CHIKV genotypes with RIG-I. (B) Bimolecular complex with IPS-1. (C) Bimolecular complex with TRAF3. (D) Bimolecular complex with TRAF6. (E) Bimolecular complex with TRIF



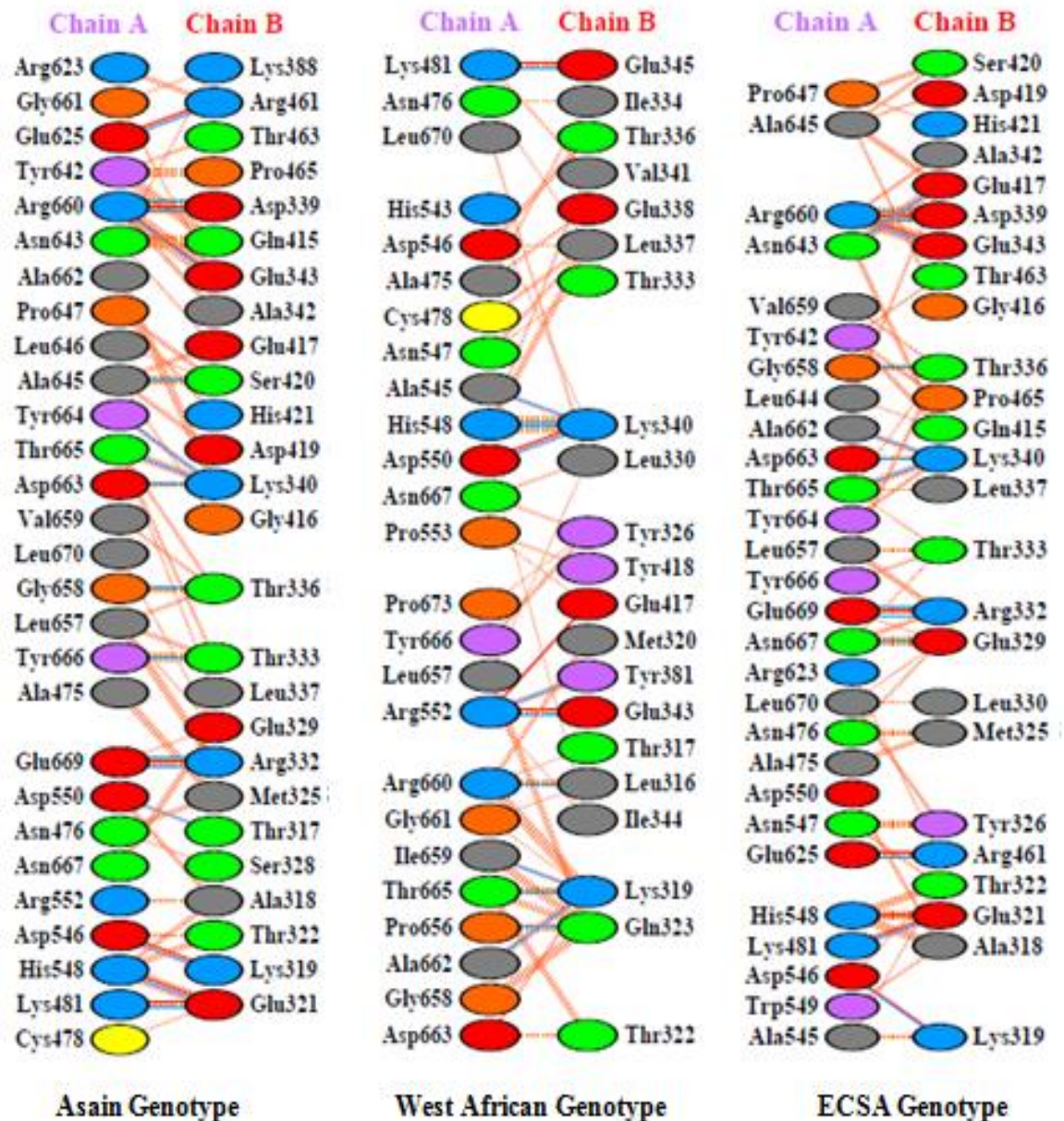
**Fig. S2:** The nsP2 protein interactions of CHIKV genotypes with human immune proteins. Chain A represented CHIKV nsP2, and Chain B represented human innate immune proteins. Highlighted bonding interactions with different colors; red color showed disulfide bond, blue color showed hydrogen bond, and orange color showed non-bonding interactions. (A) Bimolecular complex of CHIKV genotypes with RIG-I. (B) Bimolecular complex with IPS-1. (C) Bimolecular complex with TRAF3. (D) Bimolecular complex with TRAF6. (E) Bimolecular complex with TRIF.



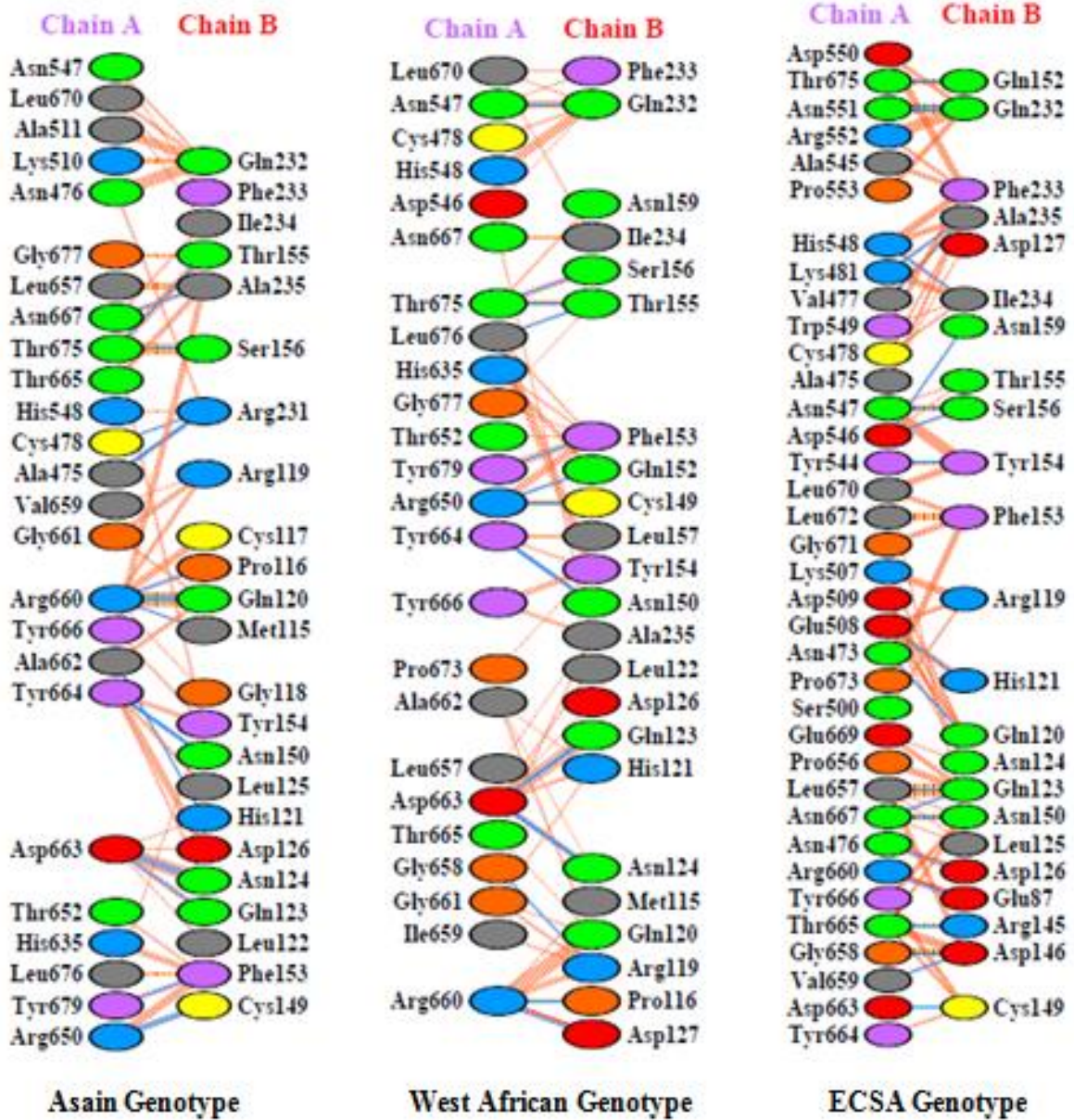
**Fig. S3:** Interacting residues among the complexes of nsP2 of various CHIKV genotypes and RIG-I. Chain A represent viral protein and chain B represent host protein. Various interactions between the two proteins are shown by different color lines; blue lines represent hydrogens bonds, red lines show salt bridges, yellow lines represent disulfide bridges and non-bonded contacts are shown by orange lines.



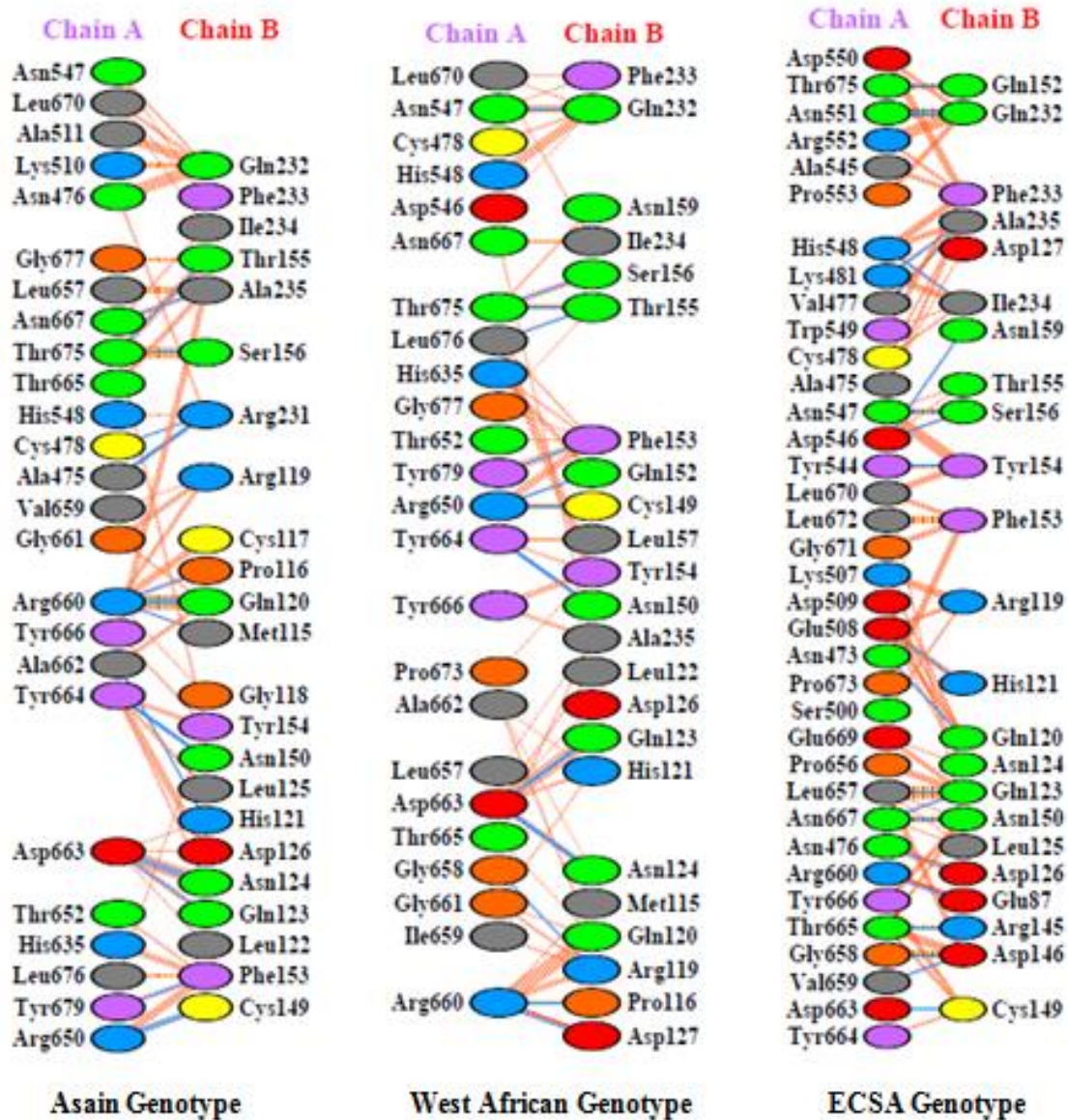
**Fig. S4:** Interacting residues among the complexes of nsP2 of various CHIKV genotypes and IPS-1. Chain A represent viral protein and chain B represent host protein. Various interactions between the two proteins are shown by different color lines; blue lines represent hydrogens bonds, red lines show salt bridges, yellow lines represent disulfide bridges and non-bonded contacts are shown by split orange lines.



**Fig. S5:** Interacting residues among the complexes of nsP2 of various CHIKV genotypes and TRAF3. Chain A represent viral protein and chain B represent host protein. Various interactions between the two proteins are shown by different color lines; blue lines represent hydrogens bonds, red lines show salt bridges, yellow lines represent disulfide bridges and non-bonded contacts are shown by split orange lines.



**Fig. S6:** Interacting residues among the complexes of nsP2 of various CHIKV genotypes and TRAF6. Chain A represent viral protein and chain B represent host protein. Various interactions between the two proteins are shown by different color lines; blue lines represent hydrogens bonds, red lines show salt bridges, yellow lines represent disulfide bridges and non-bonded contacts are shown by split orange



**Fig. S7:** Interacting residues among the complexes of nsP2 of various CHIKV genotypes and TRIF. Chain A represent viral protein and chain B represent host protein. Various interactions between the two proteins are shown by different color lines; blue lines represent hydrogens bonds, red lines show salt bridges, yellow lines represent disulfide bridges and non-bonded contacts are shown by split orange lines.