

Supplementary data for the article “Cytotoxic T-cell-based vaccine against SARS-CoV2: a hybrid immunoinformatic approach” by Alexandru Tirziu and Virgil Paunescu.

Table S1. Predictions for class I-restricted epitopes using NetMHCpan. For each peptide-HLA allele combination, the EL (eluting ligand) and BA (binding affinity) percentile rankings are given. A percentile ranking below 0.5% is considered a strong binder, while a percentile ranking below 2% is considered a weak binder.

Number	Peptide	HLA-A01:01		HLA-A26:01		HLA-A29:02		HLA-B35:01	
1	WTAGAAAYY	EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank
		0.0913	0.0166	0.0246	0.0075	0.1201	0.0261	0.6035	0.1907
2	LTDEMIAQY	HLA-A01:01		HLA-A29:02		HLA-B35:01		HLA-C07:02	
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank
		0.0014	0.0066	0.1849	0.5639	0.3419	0.5675	1.2973	3.0282
3	ATSRTLSSYY	HLA-A01:01		HLA-A11:01		HLA-B57:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.0521	0.041	0.2399	0.2605	0.6159	0.9269		
4	LPPAYTNSF	HLA-B07:02		HLA-B35:01		HLA-B53:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.4334	0.6093	0.0912	0.1476	0.1225	0.3326		
5	LSYFIASFR	HLA-A11:01		HLA-A31:01		HLA-A68:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.6634	0.1129	0.2249	0.0186	0.2393	0.009		
6	TSNQVAVLY	HLA-A26:01		HLA-B35:01		HLA-B57:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.2075	0.8458	0.2621	0.3837	0.5504	1.5585		
7	KTFPPTEPK	HLA-A03:01		HLA-A11:01		HLA-A68:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.004	0.0548	0.0023	0.0212	0.2422	0.8989		
8	VASQSIIAY	HLA-A29:02		HLA-B15:01		HLA-B35:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.2279	0.759	0.1156	0.592	0.018	0.0263		
9	GVYFASTEK	HLA-A03:01		HLA-A11:01		HLA-A68:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.0337	0.0539	0.0242	0.0265	0.793	0.9521		
10	RLFRKSNLK	HLA-A03:01		HLA-A11:01		HLA-A31:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.006	0.0078	0.1843	0.1475	0.34	0.2274		
11	TISLAGSYK	HLA-A03:01		HLA-A11:01		HLA-A68:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.3619	0.1972	0.1763	0.0678	0.534	0.204		
12	LPFNDGVYF	HLA-B07:02		HLA-B35:01		HLA-B51:01			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.6256	1.1603	0.0145	0.0108	0.199	0.1041		
13	AEIRASANL	HLA-B40:01		HLA-B44:02		HLA-B44:03			
		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.0272	0.0147	0.1568	0.1003	0.1479	0.1147		
14	CVADYSVLY	HLA-A03:01		HLA-A11:01		HLA-A68:01			

		EL_Rank	BA_Rank	EL_Rank	BA_Rank	EL_Rank	BA_Rank
		0.0321	0.0164	0.0287	0.0146	0.5368	0.5148
		HLA-A26:01		HLA-A68:01			
15	NSFTRGVYY	EL_Rank	BA_Rank	EL_Rank	BA_Rank		
		0.1743	0.3832	0.9916	1.2382		

Table S2. Predictions for class II-restricted epitopes using NetMHCIIpan. For each peptide-HLA allele combination, the percentile rankings are given. A percentile ranking below 2% is considered a strong binder, while a percentile ranking below 10% is considered a weak binder.

Number	Peptide								
1	SYYKLGASQRVAGDS	HLA-DQA1*05:01-DQB1*03:01		HLA-DRB1*01:01		HLA-DRB1*07:01			
		Rank	Rank_BA	Rank	Rank_BA	Rank	Rank_BA	Rank	Rank_BA
		1.74	2.43	1.22	0.21	1.76	1.64		
2	PINLVRDLPQGFSAL	HLA-DRB1*03:01							
		Rank	Rank_BA						
		1.45	0.07						
3	SRTLSYYKLGASQRV	HLA-DRB5*01:01		HLA-DRB5*01:02					
		Rank	Rank_BA	Rank	Rank_BA				
		0.57	0.22	0.63	0.23				
4	ITRFQTLLALHRSYL	HLA-DRB1*01:01							
		Rank	Rank_BA						
		6.24	0.87						

Table S3. Candidate synthetic long peptides and their corresponding Vaxijen score, instability index (II) and molecular weight (Mol wt).

Sequence	Vaxijen score	Conclusion	II	Mol wt (g/mol)
PINLVRDLPQGFSALLSVGGAEIRASANL	0.69	Probable ANTIGEN	32.57	3092.547
PINLVRDLPQGFSALLSVGGATSRTLSYY	0.6754	Probable ANTIGEN	25.833333	3209.648
PINLVRDLPQGFSALLSVGGTISLAGSYK	0.6082	Probable ANTIGEN	14.386667	3087.567
PINLVRDLPQGFSALLSVGGKTFPPTEPK	0.6064	Probable ANTIGEN	33.3	3192.704
PINLVRDLPQGFSALLSVGGTSNQVAVLY	0.5993	Probable ANTIGEN	15.933333	3142.602
ITRFQTLLALHRSYLLSVGGATSRTLSYY	0.5852	Probable ANTIGEN	30.263333	3401.909
ITRFQTLLALHRSYLLSVGGAEIRASAN	0.5733	Probable ANTIGEN	16.9	3171.65
SRTLSYYKLGASQRVLLSVGGTISLAGSYK	0.5715	Probable ANTIGEN	21.276667	3176.62
SRTLSYYKLGASQRVLLSVGGKTFPPTEPK	0.5698	Probable ANTIGEN	29.946667	3281.758
SRTLSYYKLGASQRVLLSVGGTSNQVAVLY	0.5626	Probable ANTIGEN	17.74	3231.656
PINLVRDLPQGFSALLSVGGVASQSIIAY	0.5599	Probable ANTIGEN	34.116667	3099.577
SRTLSYYKLGASQRVLLSVGGLPFNDGVYF	0.541	Probable ANTIGEN	23.79	3308.738
PINLVRDLPQGFSALLSVGGGVYFASTEK	0.5304	Probable ANTIGEN	19.413333	3149.593
SRTLSYYKLGASQRVLLSVGGVASQSIIAY	0.5232	Probable ANTIGEN	35.21	3188.631
SYYKLGASQRVAGDSL SVGGAEIRASANL	0.521	Probable ANTIGEN	22.63	3054.37
ITRFQTLLALHRSYLLSVGGTISLAGSYK	0.518	Probable ANTIGEN	18.183333	3279.828
ITRFQTLLALHRSYLLSVGGKTFPPTEPK	0.5163	Probable ANTIGEN	22.243333	3384.965
ITRFQTLLALHRSYLLSVGGTSNQVAVLY	0.5091	Probable ANTIGEN	19.73	3334.863
SYYKLGASQRVAGDSL SVGGATSRTLSYY	0.5064	Probable ANTIGEN	19.73	3171.471
PINLVRDLPQGFSALLSVGGLPPAYTNSF	0.496	Probable ANTIGEN	29.946667	3157.615
SRTLSYYKLGASQRVLLSVGGRLFRKSNLK	0.4954	Probable ANTIGEN	35.923333	3398.957

SRTLSYYKLGASQRVLLSVGGGVYFASTEK	0.4937	Probable ANTIGEN	30.263333	3238.647
ITRFQTLLALHRSYLLLSVGGLPFNDGVYF	0.4875	Probable ANTIGEN	20.253333	3411.945
PINLVRDLPQGFSALLLSVGGLTDEMIAQY	0.4778	Probable ANTIGEN	31.493333	3231.715
PINLVRDLPQGFSALLLSVGGLSYFIASFR	0.4777	Probable ANTIGEN	20.96	3251.773
ITRFQTLLALHRSYLLLSVGGVASQSIIAY	0.4697	Probable ANTIGEN	18.446667	3291.838
SRTLSYYKLGASQRVLLSVGGGLPPAYTNSF	0.4593	Probable ANTIGEN	25.833333	3246.669
ITRFQTLLALHRSYLLLSVGGLRFRKSNLK	0.4419	Probable ANTIGEN	16.9	3502.164
SRTLSYYKLGASQRVLLSVGGGLTDEMIAQY	0.4411	Probable ANTIGEN	31.81	3320.769
SRTLSYYKLGASQRVLLSVGGGLSYFIASFR	0.441	Probable ANTIGEN	22.766667	3340.826
ITRFQTLLALHRSYLLLSVGGGVYFASTEK	0.4402	Probable ANTIGEN	22.63	3341.854
SYKLGASQRVAGDSLLSVGGTISLAGSYK	0.4392	Probable ANTIGEN	23.083333	3049.39
SYKLGASQRVAGDSLLSVGGKTFPPTEPK	0.4375	Probable ANTIGEN	14.386667	3154.527
PINLVRDLPQGFSALLLSVGWTAGAAAYY	0.4142	Probable ANTIGEN	27.38	3121.542
SYKLGASQRVAGDSLLSVGGLPFNDGVYF	0.4087	Probable ANTIGEN	25.596667	3181.507
ITRFQTLLALHRSYLLLSVGGLPPAYTNSF	0.4058	Probable ANTIGEN	18.183333	3349.876

Table S4. Predicted synthetic long peptide (SLPs) sequences, toxicity and allergenicity prediction. Toxicity prediction was performed using ToxinPred webserver, while allergenicity was predicted using AllerCatPro.

Peptide sequence	SVM score	Conclusion	Allergenicity
PINLVRDLPQGFSALLLSVGGAEIRASANL	-1.15	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGATSRTLSYY	-1.47	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGTISLAGSYK	-1.34	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGKTFPPTEPK	-1.21	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGTSNQVAVLY	-1.63	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGATSRTLSYY	-1.25	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGAEIRASAN	-1.03	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGTISLAGSYK	-1.25	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGKTFPPTEPK	-1.15	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGTSNQVAVLY	-1.47	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGVASQSIIAY	-1.51	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGLPFNDGVYF	-1.42	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGGVYFASTEK	-1.65	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGVASQSIIAY	-1.45	Non-Toxin	No significant hit (E-value threshold 0.001)
SYKLGASQRVAGDSLLSVGGAEIRASANL	-0.99	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGTISLAGSYK	-1.15	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGKTFPPTEPK	-1.11	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGTSNQVAVLY	-1.4	Non-Toxin	No significant hit (E-value threshold 0.001)
SYKLGASQRVAGDSLLSVGGATSRTLSYY	-1.25	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGLPPAYTNSF	-1.23	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGRLFRKSNLK	-1.39	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGGVYFASTEK	-1.64	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGLPFNDGVYF	-1.4	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGLTDEMIAQY	-1.1	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGLSYFIASFR	-1.47	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGVASQSIIAY	-1.37	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSYYKLGASQRVLLSVGGGLPPAYTNSF	-1.2	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGLRFRKSNLK	-1.28	Non-Toxin	No significant hit (E-value threshold 0.001)

SRTLSEYKLGASQRVLLSVGGGLTDEMIAQY	-1	Non-Toxin	No significant hit (E-value threshold 0.001)
SRTLSEYKLGASQRVLLSVGGGLSYFIASFR	-1.4	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGGVYFASTEK	-1.49	Non-Toxin	No significant hit (E-value threshold 0.001)
SEYKLGASQRVAGDSLSSVGGTISLAGSYK	-1.02	Non-Toxin	No significant hit (E-value threshold 0.001)
SEYKLGASQRVAGDSLSSVGGKTFPPTEPK	-1.03	Non-Toxin	No significant hit (E-value threshold 0.001)
PINLVRDLPQGFSALLLSVGGWTAGAAAYY	-1.53	Non-Toxin	No significant hit (E-value threshold 0.001)
SEYKLGASQRVAGDSLSSVGGGLPFNDGVYF	-1.31	Non-Toxin	No significant hit (E-value threshold 0.001)
ITRFQTLLALHRSYLLLSVGGGLPPAYTNSF	-1.2	Non-Toxin	No significant hit (E-value threshold 0.001)

Table S5. Synthetic long peptide sequences and their best Rosetta score. MFR – most favourable regions; AAR – additional allowed regions.

Number	Peptide sequence	Residues in MFR (%)	Residues in AAR (%)	Rosetta score
1	PINLVRDLPQGFSALLLSVGGAEIRASANL	100	0	-66.335
2	PINLVRDLPQGFSALLLSVGGATSRTLSEY	100	0	-61.426
3	PINLVRDLPQGFSALLLSVGGTISLAGSYK	91.3	8.7	-65.283
4	PINLVRDLPQGFSALLLSVGGKTFPPTEPK	100	0	-64.665
5	PINLVRDLPQGFSALLLSVGGTSNQVAVLY	100	0	-67.906
6	ITRFQTLLALHRSYLLLSVGGATSRTLSEY	92.3	7.7	-52.653
7	ITRFQTLLALHRSYLLLSVGGAEIRASAN	96.2	3.8	-63.795
8	SRTLSEYKLGASQRVLLSVGGTISLAGSYK	95.8	4.2	-69.309
9	SRTLSEYKLGASQRVLLSVGGKTFPPTEPK	95.5	4.5	-68.514
10	SRTLSEYKLGASQRVLLSVGGTSNQVAVLY	96	4	-65.258
11	PINLVRDLPQGFSALLLSVGGVASQSIIAY	95.8	4.2	-56.234
12	SRTLSEYKLGASQRVLLSVGGGLPFNDGVYF	95.7	4.3	-60.258
13	PINLVRDLPQGFSALLLSVGGGVYFASTEK	100	0	-65.994
14	SRTLSEYKLGASQRVLLSVGGVASQSIIAY	100	0	-66.636
15	SEYKLGASQRVAGDSLSSVGGAEIRASANL	95.8	4.2	-51.95
16	ITRFQTLLALHRSYLLLSVGGTISLAGSYK	96	4	-52.5
17	ITRFQTLLALHRSYLLLSVGGKTFPPTEPK	95.7	4.3	-64.15
18	ITRFQTLLALHRSYLLLSVGGTSNQVAVLY	92.3	7.7	-58.35
19	SEYKLGASQRVAGDSLSSVGGATSRTLSEY	95.8	4.2	-49.082
20	PINLVRDLPQGFSALLLSVGGGLPPAYTNSF	90.9	9.1	-71.157
21	SRTLSEYKLGASQRVLLSVGGRLFRKSNLK	96	4	-62.715
22	SRTLSEYKLGASQRVLLSVGGGVYFASTEK	95.8	4.2	-65.232
23	ITRFQTLLALHRSYLLLSVGGGLPFNDGVYF	95.8	4.2	-60.78
24	PINLVRDLPQGFSALLLSVGGGLTDEMIAQY	95.8	4.2	-63.009
25	PINLVRDLPQGFSALLLSVGGGLSYFIASFR	100	0	-58.837
26	ITRFQTLLALHRSYLLLSVGGVASQSIIAY	100	0	-54.92
27	SRTLSEYKLGASQRVLLSVGGGLPPAYTNSF	95.7	4.3	-66.328
28	ITRFQTLLALHRSYLLLSVGGRLFRKSNLK	96.2	3.8	-60.846
29	SRTLSEYKLGASQRVLLSVGGGLTDEMIAQY	100	0	-66.41
30	SRTLSEYKLGASQRVLLSVGGGLSYFIASFR	96	4	-67.493
31	ITRFQTLLALHRSYLLLSVGGGVYFASTEK	96	4	-59.597
32	SEYKLGASQRVAGDSLSSVGGTISLAGSYK	91.3	8.7	-55.281
33	SEYKLGASQRVAGDSLSSVGGKTFPPTEPK	100	0	-53.123
34	PINLVRDLPQGFSALLLSVGGWTAGAAAYY	95.7	4.3	-65.343

35	SYKLGASQVRVAGDSLSSVGGLPFNDGVYF	95.5	4.5	-49.98
36	ITRFQTLALHRSYLLSVGGLPPAYTNSF	95.8	4.2	-64.887

Table S6. HADDOCK results for TLR2-SLP molecular docking (after refinement).

Complex	HADDOCK score	Van der Waals energy	Electrostatic energy	Desolvation energy	Restraints violation energy	Buried Surface Area (Å ²)
TLR2/Pep 1	-90.9 ± 0.3	-56.0 ± 2.5	-192.9 ± 16.4	3.7 ± 2.6	0.6 ± 0.2	1343.3 ± 10.2
TLR2/Pep 2	-106.4 ± 0.9	-68.1 ± 1.5	-186.4 ± 5.0	-1.1 ± 0.8	0.9 ± 0.5	1982.4 ± 33.2
TLR2/Pep 3	-85.0 ± 1.9	-51.8 ± 1.9	-200.2 ± 23.2	6.7 ± 3.6	1.6 ± 1.0	1592.2 ± 47.5
TLR2/Pep 4	-100.2 ± 1.5	-41.1 ± 4.2	-310.4 ± 13.6	3.0 ± 1.1	0.6 ± 0.2	1597.3 ± 42.7
TLR2/Pep 5	-87.9 ± 3.4	-56.8 ± 2.1	-135.7 ± 11.5	-4.0 ± 0.7	0.8 ± 0.7	1512.7 ± 42.6
TLR2/Pep 6	-125.1 ± 2.7	-72.0 ± 0.3	-210.7 ± 6.1	-11.0 ± 2.4	0.8 ± 0.5	1836.8 ± 49.8
TLR2/Pep 7	-93.9 ± 1.0	-66.0 ± 2.5	-111.3 ± 10.3	-5.7 ± 1.3	0.3 ± 0.1	1657.8 ± 15.5
TLR2/Pep 8	-116.0 ± 4.9	-58.4 ± 2.2	-289.1 ± 7.5	0.2 ± 1.7	0.8 ± 0.5	1873.1 ± 47.3
TLR2/Pep 9	-113.8 ± 2.8	-66.9 ± 2.1	-251.2 ± 2.9	3.3 ± 1.7	0.8 ± 0.2	1996.9 ± 32.2
TLR2/Pep 10	-80.4 ± 2.1	-57.8 ± 1.8	-131.3 ± 13.0	3.6 ± 3.2	1.1 ± 0.6	1527.3 ± 9.3
TLR2/Pep 11	-92.5 ± 0.8	-56.6 ± 2.4	-193.2 ± 15.1	2.6 ± 0.3	0.4 ± 0.2	1398.7 ± 12.9
TLR2/Pep 12	-122.4 ± 2.1	-69.4 ± 3.7	-272.6 ± 8.1	1.5 ± 1.5	1.0 ± 0.6	1916.3 ± 65.8
TLR2/Pep 13	-121.9 ± 1.4	-59.7 ± 3.9	-233.3 ± 16.5	-15.5 ± 1.1	0.6 ± 0.4	1921.9 ± 17.7
TLR2/Pep 14	-119.3 ± 1.2	-56.3 ± 1.6	-375.6 ± 23.6	12.0 ± 3.2	1.1 ± 0.4	1636.2 ± 37.5
TLR2/Pep 15	-107.8 ± 1.3	-65.7 ± 2.2	-173.5 ± 8.9	-7.4 ± 0.4	0.6 ± 0.2	1596.7 ± 19.6
TLR2/Pep 16	-97.1 ± 2.7	-57.4 ± 2.2	-152.4 ± 8.3	-9.3 ± 1.7	0.3 ± 0.1	1563.4 ± 66.3
TLR2/Pep 17	-100.4 ± 2.6	-59.0 ± 2.1	-231.2 ± 9.8	4.8 ± 2.4	0.6 ± 0.3	1505.1 ± 29.2
TLR2/Pep 18	-90.6 ± 1.1	-42.9 ± 2.0	-201.4 ± 13.4	-7.5 ± 3.0	0.3 ± 0.3	1288.0 ± 25.7
TLR2/Pep 19	-141.3 ± 2.8	-59.2 ± 3.0	-447.4 ± 27.2	7.3 ± 2.4	0.6 ± 0.7	1849.4 ± 23.8
TLR2/Pep 20	-73.5 ± 3.6	-55.7 ± 3.0	-93.5 ± 26.8	0.8 ± 1.5	0.4 ± 0.1	1471.0 ± 18.4
TLR2/Pep 21	-101.7 ± 1.7	-51.6 ± 4.1	-288.7 ± 26.7	7.6 ± 1.2	0.6 ± 0.2	1539.9 ± 19.4
TLR2/Pep 22	-113.3 ± 1.9	-48.5 ± 2.7	-314.0 ± 17.3	-2.2 ± 1.4	1.0 ± 0.6	1647.7 ± 14.7
TLR2/Pep 23	-130.7 ± 0.5	-65.6 ± 5.3	-216.3 ± 34.2	-22.0 ± 1.7	0.6 ± 0.1	1830.5 ± 54.5
TLR2/Pep 24	-102.4 ± 4.9	-50.8 ± 6.7	-271.9 ± 32.7	2.7 ± 1.2	0.5 ± 0.1	1478.8 ± 47.9

TLR2/Pep 25	-130.7 ± 1.6	-76.5 ± 1.0	-230.0 ± 13.3	-8.2 ± 2.5	0.6 ± 0.3	1923.1 ± 34.9
TLR2/Pep 26	-103.4 ± 1.8	-62.3 ± 4.4	-152.1 ± 4.0	-10.8 ± 2.1	0.5 ± 0.1	1853.0 ± 78.1
TLR2/Pep 27	-110.2 ± 2.8	-65.1 ± 4.7	-181.6 ± 11.8	-8.9 ± 1.6	1.1 ± 0.8	1623.3 ± 24.9
TLR2/Pep 28	-119.6 ± 2.7	-47.7 ± 3.2	-341.8 ± 11.4	-3.7 ± 1.7	0.5 ± 0.4	1584.6 ± 39.4
TLR2/Pep 29	-91.3 ± 1.3	-49.3 ± 2.2	-221.1 ± 10.3	2.1 ± 1.3	0.4 ± 0.3	1580.4 ± 26.6
TLR2/Pep 30	-126.2 ± 0.8	-69.0 ± 2.6	-258.1 ± 13.9	-5.6 ± 0.6	0.6 ± 0.6	1915.4 ± 34.8
TLR2/Pep 31	-135.5 ± 3.0	-63.4 ± 2.7	-317.5 ± 22.6	-8.6 ± 1.9	0.4 ± 0.2	1767.9 ± 32.0
TLR2/Pep 32	-97.9 ± 2.0	-39.3 ± 4.4	-284.3 ± 28.9	-1.8 ± 1.1	0.5 ± 0.2	1235.6 ± 12.3
TLR2/Pep 33	-110.5 ± 3.1	-62.2 ± 4.1	-239.6 ± 17.7	-0.5 ± 1.7	0.7 ± 0.2	1769.4 ± 22.4
TLR2/Pep 34	-94.0 ± 2.4	-63.5 ± 3.2	-117.9 ± 13.6	-7.0 ± 1.7	0.7 ± 0.4	1599.6 ± 52.5
TLR2/Pep 35	-137.3 ± 3.8	-51.9 ± 3.5	-471.3 ± 9.2	8.8 ± 2.3	0.8 ± 0.4	1989.9 ± 60.4
TLR2/Pep 36	-98.2 ± 4.3	-58.6 ± 4.0	-130.8 ± 12.6	-13.5 ± 2.0	0.7 ± 0.5	1495.2 ± 36.6

Table S7. HADDOCK results for TLR4-SLP molecular docking (after refinement).

Complex	HADDOCK score	Van der Waals energy	Electrostatic energy	Desolvation energy	Restraints violation energy	Buried Surface Area (Å ²)
TLR4/Pep1	-87.7 ± 1.2	-48.2 ± 1.8	-95.1 ± 12.5	-20.7 ± 0.6	1.8 ± 0.9	1250.5 ± 7.4
TLR4/Pep2	-109.9 ± 1.1	-54.4 ± 2.4	-154.5 ± 11.4	-24.8 ± 1.1	1.2 ± 0.4	1299.9 ± 30.8
TLR4/Pep3	-97.0 ± 0.8	-60.2 ± 1.5	-67.1 ± 12.1	-23.6 ± 1.3	2.4 ± 0.9	1349.3 ± 12.0
TLR4/Pep4	-90.8 ± 0.7	-48.9 ± 1.8	-77.1 ± 9.8	-26.6 ± 1.0	1.0 ± 0.5	1135.0 ± 32.3
TLR4/Pep5	-97.3 ± 0.7	-57.2 ± 2.6	-110.9 ± 7.8	-18.0 ± 1.8	1.3 ± 0.2	1407.2 ± 25.3
TLR4/Pep6	-122.7 ± 1.0	-64.4 ± 1.6	-152.7 ± 13.8	-27.9 ± 1.3	1.6 ± 0.4	1422.5 ± 35.7
TLR4/Pep7	-113.5 ± 0.5	-52.7 ± 1.6	-135.6 ± 9.8	-33.7 ± 1.1	0.9 ± 0.4	1345.7 ± 12.6
TLR4/Pep8	-102.8 ± 2.4	-55.4 ± 2.9	-137.6 ± 12.6	-20.0 ± 1.6	1.3 ± 0.6	1229.5 ± 17.7
TLR4/Pep9	-108.9 ± 3.7	-56.3 ± 3.5	-170.6 ± 23.3	-18.6 ± 1.7	1.5 ± 0.5	1378.0 ± 20.9
TLR4/Pep10	-98.1 ± 5.9	-52.7 ± 3.9	-103.1 ± 19.4	-25.0 ± 1.1	1.8 ± 0.5	1361.8 ± 35.5
TLR4/Pep11	-80.8 ± 0.8	-48.9 ± 1.7	-82.6 ± 14.1	-15.5 ± 1.1	1.2 ± 0.3	1195.2 ± 37.6
TLR4/Pep12	-128.7 ± 1.3	-59.8 ± 3.9	-186.9 ± 16.5	-31.7 ± 2.1	1.4 ± 0.3	1421.4 ± 32.2
TLR4/Pep13	-112.2 ± 1.4	-57.5 ± 4.4	-124.1 ± 14.8	-30.1 ± 1.5	2.0 ± 0.2	1548.8 ± 35.0
TLR4/Pep14	-109.9 ± 0.7	-56.2 ± 0.6	-173.3 ± 8.7	-19.1 ± 1.0	1.1 ± 0.4	1325.4 ± 27.0
TLR4/Pep15	-119.9 ± 5.0	-55.4 ± 4.5	-257.3 ± 41.8	-13.2 ± 2.1	1.8 ± 0.2	1409.5 ± 15.0
TLR4/Pep16	-109.6 ± 1.6	-49.0 ± 1.3	-192.8 ± 10.8	-22.1 ± 1.0	1.2 ± 0.6	1465.0 ± 23.0
TLR4/Pep17	-125.2 ± 1.6	-51.9 ± 2.2	-224.9 ± 14.0	-28.5 ± 1.8	1.5 ± 0.3	1304.1 ± 34.2
TLR4/Pep18	-100.9 ± 0.7	-52.9 ± 0.3	-92.0 ± 2.8	-29.7 ± 0.5	1.0 ± 0.2	1321.4 ± 26.2
TLR4/Pep19	-129.0 ± 1.5	-73.1 ± 2.2	-152.2 ± 9.9	-25.6 ± 3.2	1.2 ± 0.6	1780.1 ± 43.9
TLR4/Pep20	-84.0 ± 2.0	-51.8 ± 1.6	-56.8 ± 5.2	-20.9 ± 1.0	0.8 ± 0.2	1129.6 ± 36.7
TLR4/Pep21	-105.4 ± 2.8	-54.5 ± 1.0	-152.8 ± 11.2	-20.5 ± 2.2	2.2 ± 0.9	1347.1 ± 25.0
TLR4/Pep22	-108.2 ± 5.2	-50.3 ± 1.2	-164.4 ± 23.9	-25.1 ± 0.9	0.8 ± 0.3	1199.0 ± 34.2

TLR4/Pep23	-121.8 ± 0.6	-52.9 ± 1.4	-155.8 ± 6.3	-37.8 ± 0.2	1.4 ± 0.3	1371.0 ± 8.7
TLR4/Pep24	-95.6 ± 0.5	-47.3 ± 2.0	-145.8 ± 12.2	-19.2 ± 1.6	1.4 ± 0.6	1169.3 ± 11.8
TLR4/Pep25	-116.9 ± 1.8	-67.8 ± 1.8	-85.3 ± 6.5	-32.1 ± 1.6	1.1 ± 0.4	1421.9 ± 24.0
TLR4/Pep26	-115.6 ± 2.1	-64.0 ± 2.7	-39.0 ± 2.2	-43.9 ± 0.8	1.5 ± 0.4	1317.9 ± 44.4
TLR4/Pep27	-107.0 ± 1.6	-48.9 ± 0.8	-159.3 ± 11.3	-26.3 ± 2.2	1.1 ± 0.4	1271.2 ± 22.1
TLR4/Pep28	-116.1 ± 0.4	-59.2 ± 1.1	-135.0 ± 10.8	-29.9 ± 1.9	0.8 ± 0.3	1390.9 ± 19.4
TLR4/Pep29	-106.5 ± 1.6	-57.4 ± 2.6	-122.0 ± 9.4	-24.8 ± 1.6	1.4 ± 0.6	1293.1 ± 20.9
TLR4/Pep30	-113.9 ± 0.5	-58.1 ± 1.3	-73.2 ± 11.5	-41.2 ± 1.2	0.9 ± 0.3	1301.3 ± 21.1
TLR4/Pep31	-102.9 ± 0.7	-42.2 ± 1.9	-158.9 ± 9.2	-29.1 ± 1.8	1.4 ± 0.7	1155.5 ± 15.1
TLR4/Pep32	-122.0 ± 1.1	-65.9 ± 0.8	-186.0 ± 10.0	-18.9 ± 0.7	0.9 ± 0.3	1288.1 ± 13.5
TLR4/Pep33	-120.8 ± 3.1	-61.0 ± 5.2	-140.4 ± 16.3	-31.8 ± 1.3	1.4 ± 0.4	1368.2 ± 43.1
TLR4/Pep34	-130.8 ± 4.5	-69.5 ± 2.6	-108.3 ± 7.7	-39.7 ± 1.6	1.2 ± 0.5	1587.9 ± 38.8
TLR4/Pep35	-144.2 ± 1.6	-68.6 ± 2.2	-242.2 ± 17.9	-27.4 ± 1.9	1.7 ± 0.7	1659.2 ± 22.7
TLR4/Pep36	-105.7 ± 1.8	-55.7 ± 1.0	-153.7 ± 14.5	-19.4 ± 0.7	1.5 ± 0.5	1369.9 ± 32.4

Table S8. Predicted ΔG and K_d for the TLR2/4-SLP interactions using PRODIGY.

Complex	$\Delta G(\text{kcal/mol})$	$K_d(\text{M})$ at 37.0 °C	Complex	$\Delta G(\text{kcal/mol})$	$K_d(\text{M})$ at 37.0 °C
TLR2/Pep1	-9.7	1.5×10^{-7}	TLR4/Pep1	-9	4.9×10^{-7}
TLR2/Pep2	-12.5	1.6×10^{-9}	TLR4/Pep2	-10.4	4.6×10^{-8}
TLR2/Pep3	-11.8	4.6×10^{-9}	TLR4/Pep3	-11.3	1.0×10^{-8}
TLR2/Pep4	-10.8	2.3×10^{-8}	TLR4/Pep4	-8.9	5.5×10^{-7}
TLR2/Pep5	-12	3.5×10^{-9}	TLR4/Pep5	-11.4	9.1×10^{-9}
TLR2/Pep6	-10.9	1.9×10^{-8}	TLR4/Pep6	-10.1	7.3×10^{-8}
TLR2/Pep7	-10.7	2.6×10^{-8}	TLR4/Pep7	-9.6	1.7×10^{-7}
TLR2/Pep8	-11.5	8.1×10^{-9}	TLR4/Pep8	-10.8	2.5×10^{-8}
TLR2/Pep9	-11.7	5.7×10^{-9}	TLR4/Pep9	-9.7	1.4×10^{-7}
TLR2/Pep10	-11.2	1.4×10^{-8}	TLR4/Pep10	-9.5	2.1×10^{-7}
TLR2/Pep11	-10	8.3×10^{-8}	TLR4/Pep11	-10.8	2.6×10^{-8}
TLR2/Pep12	-13	7.1×10^{-10}	TLR4/Pep12	-9.8	1.3×10^{-7}
TLR2/Pep13	-12.2	2.5×10^{-9}	TLR4/Pep13	-11.5	7.9×10^{-9}
TLR2/Pep14	-11.9	4.0×10^{-9}	TLR4/Pep14	-10.2	6.7×10^{-8}
TLR2/Pep15	-12	3.5×10^{-9}	TLR4/Pep15	-10.8	2.5×10^{-8}
TLR2/Pep16	-11.6	7.1×10^{-9}	TLR4/Pep16	-9.7	1.4×10^{-7}
TLR2/Pep17	-10.9	2.2×10^{-8}	TLR4/Pep17	-9.5	2.1×10^{-7}
TLR2/Pep18	-9.9	1.1×10^{-7}	TLR4/Pep18	-10.8	2.4×10^{-8}
TLR2/Pep19	-11.6	6.9×10^{-9}	TLR4/Pep19	-12.3	2.2×10^{-9}
TLR2/Pep20	-11.2	1.3×10^{-8}	TLR4/Pep20	-9.2	3.1×10^{-7}
TLR2/Pep21	-10.8	2.4×10^{-8}	TLR4/Pep21	-10.5	3.7×10^{-8}
TLR2/Pep22	-11.1	1.4×10^{-8}	TLR4/Pep22	-10.6	3.4×10^{-8}
TLR2/Pep23	-11.8	4.5×10^{-9}	TLR4/Pep23	-9.8	1.1×10^{-7}
TLR2/Pep24	-10.4	4.7×10^{-8}	TLR4/Pep24	-9.4	2.2×10^{-7}
TLR2/Pep25	-12.8	9.1×10^{-10}	TLR4/Pep25	-12.8	9.1×10^{-10}
TLR2/Pep26	-12.3	2.2×10^{-9}	TLR4/Pep26	-9.3	2.7×10^{-7}
TLR2/Pep27	-13.3	4.5×10^{-10}	TLR4/Pep27	-10	8.6×10^{-8}
TLR2/Pep28	-11.5	7.7×10^{-9}	TLR4/Pep28	-9.7	1.4×10^{-7}
TLR2/Pep29	-11.4	9.0×10^{-9}	TLR4/Pep29	-10.7	2.9×10^{-8}
TLR2/Pep30	-13.1	6.1×10^{-10}	TLR4/Pep30	-10.6	3.2×10^{-8}
TLR2/Pep31	-11.2	1.3×10^{-8}	TLR4/Pep31	-9.2	3.2×10^{-7}
TLR2/Pep32	-10.1	8.0×10^{-8}	TLR4/Pep32	-9.7	1.4×10^{-7}
TLR2/Pep33	-10.6	3.1×10^{-8}	TLR4/Pep33	-10.1	8.0×10^{-8}

TLR2/Pep34	-12.1	2.9×10^{-9}	TLR4/Pep34	-12.5	1.5×10^{-9}
TLR2/Pep35	-12.5	1.6×10^{-9}	TLR4/Pep35	-10.5	3.7×10^{-8}
TLR2/Pep36	-11	1.7×10^{-8}	TLR4/Pep36	-10.7	3.1×10^{-8}