

Figure S1: Graphical representation of secondary structure of protein vaccine was obtained from PSIPRED server. The blue bars show confidence of prediction. The two α -helix regions that were imposed to 3D structure of vaccine are shown in the dashed box (residues 170-178 and 286-293).

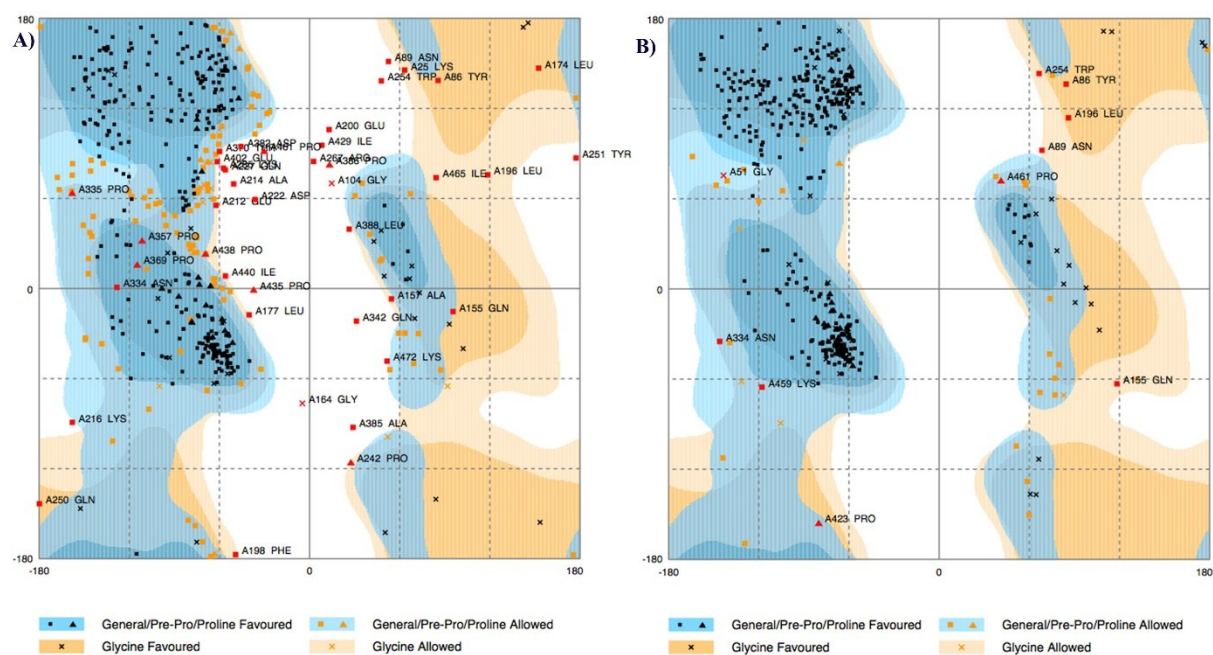


Figure S2: Validation of the initial and refined 3D model of protein vaccine. A) In the initial model 328 (67.8%), 115(23.8%) and 41 (8.5%) of residues are located in favored, allowed and outlier regions, respectively. B) In the refined model, 444 (91.7%), 30 (6.2%) and only 10 (2.1%) of residues are located in favored, allowed and outlier regions, respectively.

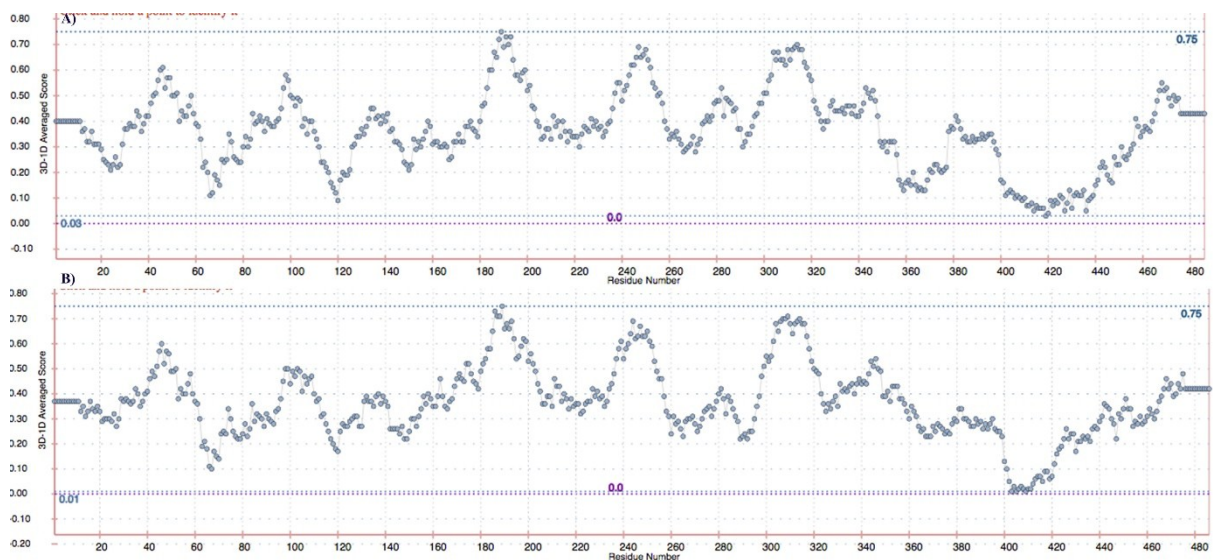


Figure S3: Verify 3D evaluation of the initial and refined 3D model of protein vaccine. A) In the initial model 85.80% of the residues had an average 3D-1D score ≥ 0.2 . B) In the refined model 92.8% of the residues had an average 3D-1D score ≥ 0.2 .

Z-Score: **-9.05**

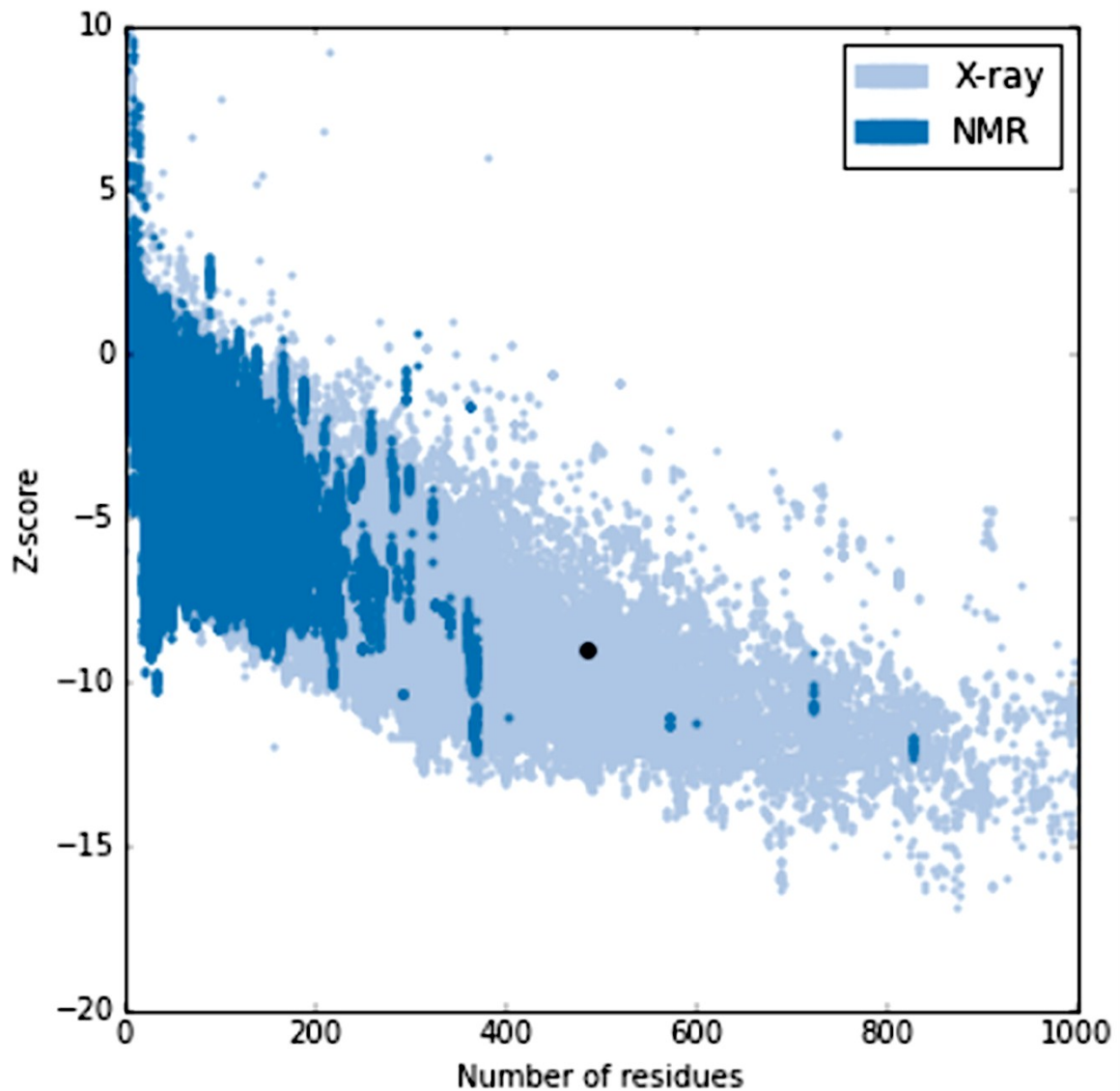


Figure S4: The ProSA *z*-score represents overall quality of protein vaccine. The *z*-score of primary model was not defined due to low quality, but the *z*-score of refined model is -9.05 (in the plot), which shows our structure is within the range of scores typically found for native proteins of similar size. The *z*-score of refined model is delineated in large black spot. The *z*-Score plot consists of *z*-scores of all experimentally protein chains in PDB determined by NMR spectroscopy (dark blue) and X-ray crystallography (light blue).

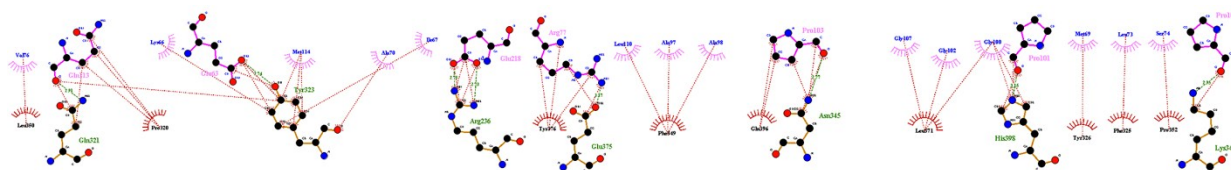


Figure S5: LigPlot⁺2D depiction of intermolecular interactions between the protein vaccine (LT-IIc) and TLR2. Binding of LT-IIc to TLR2 is mostly mediated by hydrophobic interactions and a possible hydrogen bond between residues Q321, Y323, R236, E375, N345, H398, and K347 of TLR2 (green) and residues Q113, E63, E218, R77, P103, P101 and P105 of LT-IIc (blue). The projected hydrophobic interactions include L350, P320, Y323, R236, Y376, E375, F349, Q396, N345, L371, H398, Y326, F325, P352 and K347 of TLR2 and residues V76, Q113, K66, E63, M114, A70, I67, E218, R77, L110, A97, A98, P103, G107, G102, G100, P101, M69, L73, S74 and P105 of LT-IIc.

Key

----- = Hydrogen bond and its length

----- = Hydrophobic interactions

●● Ligand bond
●● Non-ligand bond

His 53 Non-ligand residues involved in hydrophobic contact(s)
● Corresponding atoms involved in hydrophobic contact(s)

Table S1: The high-scored peptide regions over MHC-II alleles correspond to HP0487 and HP0906 antigens, were selected according to results of MHCpreds, IEDB and RANKPEP.

Servers	Antigens		Best ranked epitope in the region
MHCpreds	Start aa	End aa	Predicted IC ₅₀ value (nM) ^a
	HP0487		
	23	41	6.14
	74	118	6.11
	201	265	6.10
	366	419	6.11
	438	471	6.11
	HP0906		
	4	42	5.88
	77	116	5.9
	160	208	6.1
	299	333	6.11
	365	442	5.89
	493	525	6.12
IEDB			Percentile rank ^b
	HP0487		
	33	48	3.74
	89	113	0.25
	141	173	2.52
	193	241	0.52
	283	328	0.58
	387	401	16.89
	HP0906		
	2	21	3.11
	96	115	16.3
	215	232	3.27
	274	343	2.35
	400	423	1.1
	513	527	3.16
RANKPEP			Score ^c
	HP0487		
	22	70	11.84
	95	171	19.36
	221	274	19.36
	286	314	13.29
	393	435	20.24
	HP0906		
	3	35	11.94
	78	125	20.35
	156	184	13.37

	289	346	22.40
	392	415	21.75
	498	527	17.24

^a Low predicted IC₅₀ value=good binder.

Servers	Antigens		Best ranked epitope in the region
Bcpreds*	Start aa	End aa	Score ^a
	HP0487		
	60	80	0.76
	113	133	1
	178	198	0.96
	207	227	0.99
	260	280	0.99
	294	314	0.93
	336	356	0.99
	389	409	0.92
	440	460	1
	HP0906		
	2	20	0.97
	22	42	0.98
	46	87	0.99
	95	115	0.97
	124	187	1
	226	246	0.89
	263	374	1
	393	413	0.94
	478	498	0.99
	505	525	0.98
ABCpred*			Score ^a
	HP0487		
	10	30	0.85
	46	110	0.88
	133	153	0.85
	185	224	0.9
	264	284	0.81
	338	358	0.89
	385	405	0.88
	446	466	0.89
	HP0906		
	13	52	0.8
	94	114	0.92

	139	156	0.79
	270	290	0.8
	361	399	0.86
	407	454	0.91
	495	528	0.87
BepiPred			Score ^a
	HP0487		
	63	77	1.43
	107	130	2.47
	176	187	1.41
	213	218	1.35
	266	277	1.44
	295	299	1.2
	333	352	1.04
	396	404	1.89
	HP0906		
	2	38	1.91
	54	102	2.17
	130	188	2.39
	258	277	1.89
	315	325	2.25
	336	392	2.66
	403	411	1.17
	486	500	2.52
	505	520	2.06

^b Low percentile=good binder.

^c High score=good binder.

Table S2: The high-scored peptide regions of HP0487 and HP0906 antigens, were selected by Bcpreds, ABCpred and BepiPred servers as linear B-cell epitopes.

^a Higher score= higher probability to be as linear B-cell epitope

*In Bcpreds and ABCpred the highest score for epitopes=1