

Table S4. The binding free energies (ΔG) in kcal/mol computed by both molecular mechanics generalized Born surface area (MM-GBSA) and molecular mechanics Poisson-Boltzmann surface area (MM-PBSA) methods at TLR4/TLR4* interface.

Complex	#	Generalized Born (GB)				Poisson-Boltzmann (PB)			
		ΔE_{MM}		ΔG_{sol}		ΔG	ΔG_{sol}		ΔG
		ΔE_{ele}	ΔE_{vdw}	ΔG_{pol}	ΔG_{nonpol}		ΔG_{pol}	ΔG_{nonpol}	
(TLR4-MD2) ₂	1	-147.29 (66.89)	-44.66 (5.57)	186.86 (63.12)	-8.38 (0.85)	-13.44 (8.31)	161.34 (62.61)	-7.27 (0.59)	-37.86 (11.92)
(TLR4-MD2) ₂	2	-78.99 (35.49)	-42.97 (8.41)	115.25 (36.00)	-7.44 (1.27)	-14.13 (6.74)	89.17 (36.79)	-6.25 (0.93)	-39.01 (9.77)
(TLR4-MD2) ₂	3	-47.99 (29.34)	-31.50 (5.81)	70.24 (28.23)	-5.38 (0.62)	-14.60 (4.58)	48.45 (27.68)	-4.49 (0.48)	-35.50 (6.21)
(TLR4-MD2) ₂	4	-228.82 (56.02)	-50.39 (8.15)	259.70 (52.92)	-9.03 (1.32)	-28.51 (10.42)	239.53 (52.13)	-7.39 (0.85)	-47.04 (13.89)
(TLR4-MD2) ₂	1-4	-125.77 (80.25)	-42.38 (7.92)	158.01 (83.08)	-7.56 (1.59)	-17.67 (7.24)	134.62 (84.09)	-6.35 (1.34)	-39.85 (5.01)
(TLR4-MD2-LPS) ₂	1	258.48 (40.74)	-66.02 (12.20)	-183.62 (45.31)	-8.44 (1.89)	0.41 (9.09)	-210.06 (44.72)	-7.86 (1.35)	-25.45 (10.80)
(TLR4-MD2-LPS) ₂	2	235.55 (51.41)	-72.36 (10.04)	-154.92 (52.59)	-9.98 (1.50)	-1.69 (9.70)	-181.06 (51.49)	-9.04 (0.97)	-26.89 (12.54)
(TLR4-MD2-LPS) ₂	3	251.44 (42.44)	-65.73 (9.10)	-172.15 (41.01)	-8.93 (1.49)	4.64 (9.55)	-199.63 (41.30)	-8.41 (0.99)	-22.31 (11.39)
(TLR4-MD2-LPS) ₂	4	223.79 (44.69)	-75.54 (8.99)	-142.75 (44.48)	-10.26 (1.26)	-4.75 (9.57)	-171.05 (43.93)	-9.13 (0.84)	-31.93 (12.35)
(TLR4-MD2-LPS) ₂	1-4	242.32 (15.64)	-69.91 (4.84)	-163.36 (18.11)	-9.40 (0.86)	-0.35 (3.94)	-190.45 (17.64)	-8.61 (0.59)	-26.65 (4.01)
(TLR4-MD2-neoseptin3) ₂	1	276.68 (32.65)	-71.64 (6.42)	-201.17 (32.90)	-8.65 (0.98)	-4.77 (6.25)	-231.08 (32.95)	-7.65 (0.80)	-33.67 (7.93)
(TLR4-MD2-neoseptin3) ₂	2	195.57 (51.16)	-91.74 (8.11)	-108.87 (50.33)	-12.63 (1.21)	-17.65 (9.71)	-139.57 (50.43)	-10.57 (0.77)	-46.29 (12.39)
(TLR4-MD2-neoseptin3) ₂	3	240.33 (56.26)	-80.70 (12.34)	-160.99 (59.32)	-10.42 (2.15)	-11.77 (10.53)	-190.45 (59.26)	-8.92 (1.53)	-39.73 (11.59)
(TLR4-MD2-neoseptin3) ₂	4	255.73 (45.09)	-80.25 (10.65)	-173.19 (48.01)	-10.23 (1.77)	-7.93 (9.15)	-197.95 (47.12)	-8.87 (1.35)	-31.33 (11.77)
(TLR4-MD2-neoseptin3) ₂	1-4	242.08 (34.40)	-81.08 (8.24)	-161.06 (38.64)	-10.48 (1.64)	-10.53 (5.54)	-189.76 (37.83)	-9.00 (1.20)	-37.76 (6.70)