

Table S9. The key residues of TLR4 and TLR4* identified by per-residue free energy decomposition (kcal/mol) in the TLR4/TLR4* interface of ligand-free (TLR4-MD2)₂ tetramer, lipopolysaccharide (LPS)-bound (TLR4-MD2-LPS)₂ tetramer, and neoseptin3-bound (TLR4-MD2-neoseptin3)₂ tetramer complexes. The values are averaged over the 1000 frames of the combined 4 trajectories of each system. A negative value is a favorable free energy, while a positive value is an unfavorable. The shaded entries are those that have unfavorable free energy contribution of 2.0 kcal/mol or greater.

		Complex		
		(TLR4-MD2) ₂	(TLR4-MD2-LPS) ₂	(TLR4-MD2-neoseptin3) ₂
Monomer	Residue	TLR4/TLR4* Interface		
TLR4	S364	-0.034	-1.206	-1.322
	A409	-0.324	-1.309	-2.113
	K433	-6.737	3.183	0.885
	R434	-2.979	-0.282	-0.244
	E507	0.444	2.684	1.154
TLR4*	S364	-0.026	-1.221	-2.314
	A409	-0.247	-1.324	-1.673
	K433	-4.672	2.538	2.376
	R434	-6.015	-0.293	-0.242
	E507	0.386	2.548	1.647