Supporting Information

Table S1. Binding sites of CD147 obtained from MOE (Site Finder).

Binding Sites.	Residues
Site1	S78 D79 D80 Q81 W82 G83 Q100 L101 HID102 G103 P104 P105 R106 E129 S130 V131 P132 S193 D194
Site2	A109 V110 K111 E114 M123 L124 V125 I198
Site3	W137 A138 W139 L150 M151 N152 V160 N186
Site4	R106 V107 K108 K127 S128 E129 Q164 G165 R166
Site 5	HIP53 W55 L62 E64 L67 K71 T72 E73
Site 6	L38 L62 E73 F74 K75
Site 7	K57 V61 F74 D80 W82 Y85
Site 8	I37 Q81 Q100 L101 HID102 G103 P104 N44
Site 9	K57 W82 G83 E84 Q100 E129

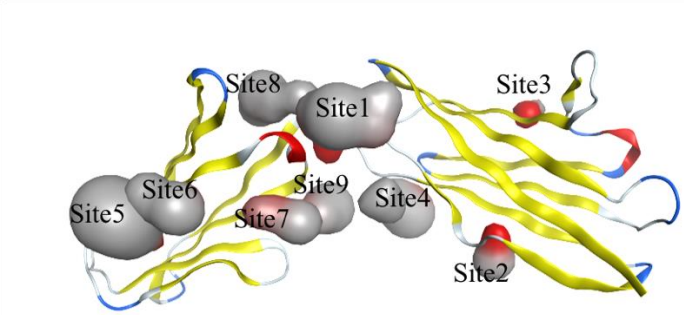

Figure S1. Binding sites of CD147 protein obtained from MOE (Site Finder).

Table S2. Binding sites of α7nAChr obtained from MOE (Site Finder).

Binding Sites	Conformation	Residues
Site1	Desensitized	(K45 N46 Q47 S126 C127 A257 E258 M260 P261 A262 T263) and (Q38 I39 M40 D41 V42 D43 E44 K45 F134 P169 N170 G171 E172 W173 R205 Y209 Y210 N213 L214 L255 V256 E258 I259 M260)
Site2	Desensitized	Y7 R78 F79 P80 D81 F103 H04 T105 N106) and (P16 L17 E18 L55 M57 D81 I84 W85 K86 P87 D88 I89 L90 D100 T102 H04 Y117 P119 S149 Y150
Site3	Desensitized	(Y92 S147 W148 S149 Y150 W153 Y187 C189 C190 K191 E192 Y194) and (W54 T76 R78 T105 N106 V107 L108 N110 Q116 Y117 L118 P119)
Site4	Desensitized	(Q47 Y92 N93 S126 C127 Y128 H40 C141 K142 K144 Y187 T200) and (L37 Q38 N52 W54 I168 P169 N170)
Site 1	Activated	(K45 N46 Q47 V48 A95 E97 K124 S126 C127 Y128 M253 L254 A257 E258 M260 P261 A262 T263) and (Q38 I39 M40 D41 V42 D43 E44 K45 T50 I122 I168 P169 N170 E172 W173 R205 Y209 Y210 N213 L214 F252 L255 E258 I259 M260)
Site 2	Activated	(R19 D24 S25 Q26 P27 Y92 S147 W148 S149 G151 W153 S154 Y187 C189 C190 K191 E192 Y194) and (Q3 W54 G73 V74 K75 T76 R78 T105 N106 L108 N110 Q116 Y117 L118 P119)
Site 3	Activated	(P16 L17 M57 D81 G82 I84 W85 K86 P87 D88 I89 L90 D100 T102 H04 Y117 P119 W148 S149 Y150) and (Y7 R78 F79 P80 F103 H04 T105 N106)
Site 4	Activated	(V287 I290 V291 Y294 HID295 P299 D300 G302 K303 P305 T308 R309 L312 E436 W437 A440 V444)
Site 1	Resting	(P16 L17 R19 D24 S25 Q26 P27 L55 M57 D81 G82 I84 W85 K86 P87 D88 I89 L90 Y92 D100 T102 HIP104 Y117 P119 S147 W148 S149 Y150 G151 W153 S154

		Y187 C189 C190 E192 Y194) and (Q3 Y7 G73 V74 K75 T76 V77 R78 F103 T105 N106 L108 Q116 Y117 L118)
Site 2	Resting	(Q3 G73 V74 K75 T76 R78 T105 N106 L108 Q116 Y117 L118) and (R19 D24 S25 Q26 P27 Y92 S147 W148 S149 Y150 G151 W153 S154 Y187 C189 C190 E192 Y194)
Site 3	Resting	(P16 L17 L55 M57 D81 G82 I84 W85 K86 P87 D88 I89 L90 D100 T102 HIP104 Y117 P119 W148 S149 Y150) and (Y7 R78 F103 HIP104 T105 N106)

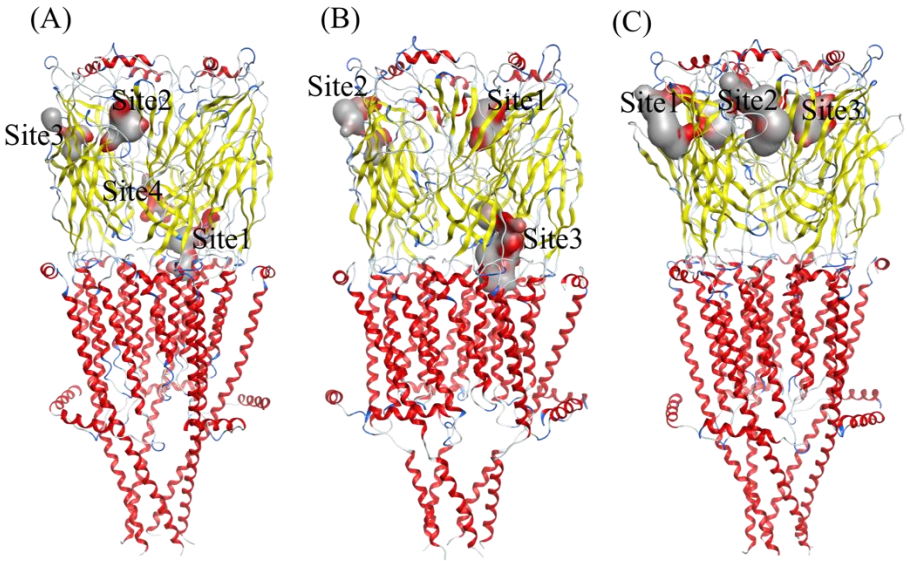

Figure S2. Binding sites of (**A**) desensitized, (**B**) activated and (**C**) resting conformations of α7nAChr protein obtained from MOE (Site Finder).

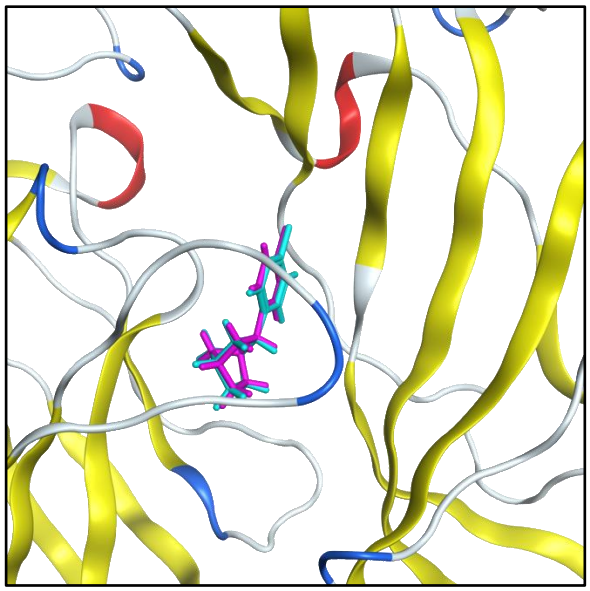

Figure S3. Positive control docking of Epibatidine of (PDB:7KOX) of the α7nAChr receptor. Experimental pose of Epibatidine is depicted in purple, while the docking pose is shown in cyan.

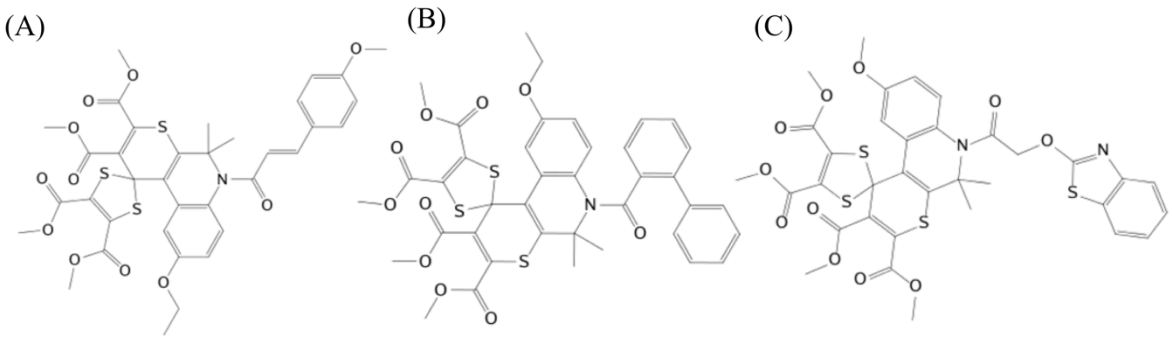

Figure S4. Decoy compounds.

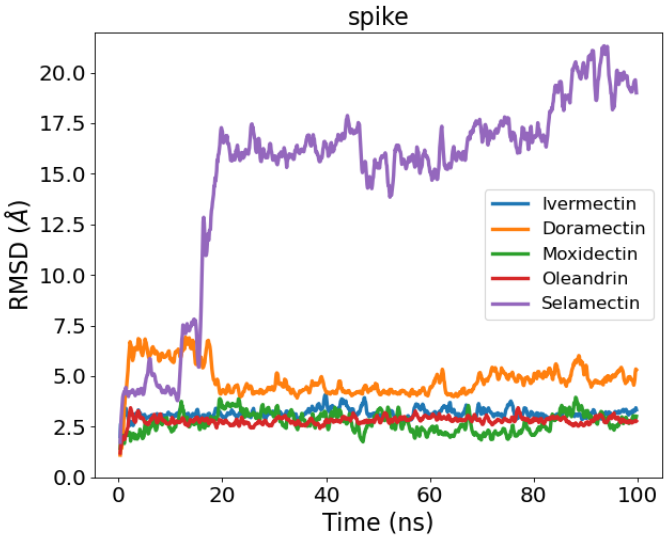

Figure S5. Time-evolution of the RMSD of top-ranked inhibitors with respect to spike.

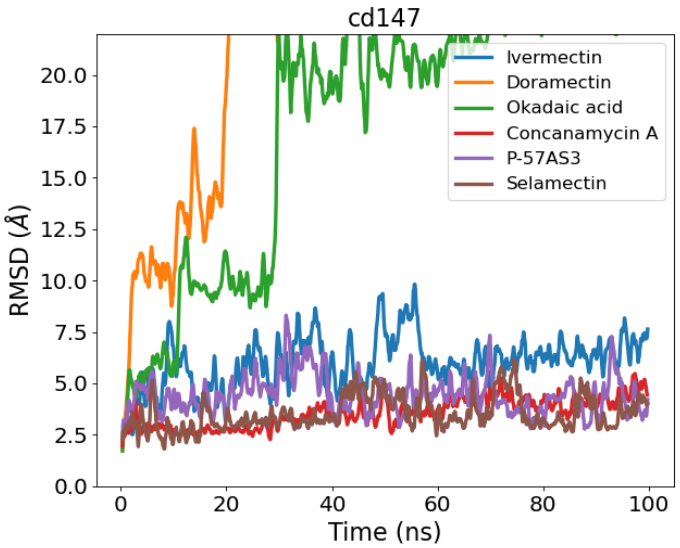

Figure S6. Time-evolution of the RMSD of top-ranked inhibitors with respect to the CD147 receptor.

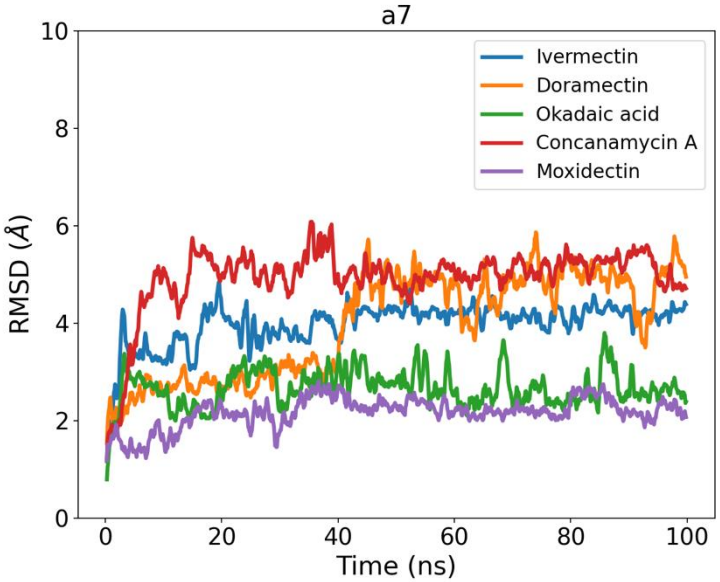

Figure S7. Time-evolution of the RMSD of top-ranked inhibitors with respect to the $\alpha 7$nAChr receptor.

Table S3. Results of the docking analysis of Ivermectin for spike protein S1 on all binding sites on NTD and RBD in open and closed positions. The highest S-Score (in absolute value) was obtained for NTD Site 10, in the open position.

Open				Closed			
NTD		RBD		NTD		RBD	
Score (kcal/mol)	Site	Score (kcal/mol)	site	Score (kcal/mol)	Site	Score (kcal/mol)	Site
-6.973	Site 1	-6.578	site 16	-7.045	Site 1	-6.46	site 16
-7.561	Site 2	-8.256	site 17	-7.175	Site 2	-6.743	site 17
-7.028	Site 3	-6.144	site 18	-7.183	Site 3	-6.748	site 18
-7.441	Site 4	-8.239	site 19	-8.205	Site 4	-6.424	site 19
-7.412	Site 5	-8.209	site 20	0	Site 5	-6.603	site 20
-7.522	Site 6	-7.813	site 21	-7.246	Site 6	-6.856	site 21
-6.343	Site 7	-7.513	site 22	-6.031	Site 7	-7.735	site 22
-5.794	Site 8			-6.308	Site 8		
-6.735	Site 9			-6.913	Site 9		
-8.948	Site 10			-7.497	Site 10		
-6.955	Site 11			-7.032	Site 11		
-6.149	Site 12			-6.258	Site 12		
-7.057	Site 13			0	Site 13		
-7.108	Site 14			-6.67	Site 14		
-7.663	Site 15			-7.081	Site 15		

Table S4. Results of the docking analysis of Ivermectin on all sites of CD147.

CD147	
Score (kcal/mol)	**Site**
-7.527	site 5
-7.468	site 2
-7.436	site 6
-7.233	site 12
-7.136	site 1
-6.943	site 8
-6.758	site 9
-6.745	site 7
-6.703	site 4
-6.611	site 3
-6.379	site 11
-6.356	site 10

Table S5. Results of the docking analysis of Ivermectin on all sites of α7nAChr. Different values for one site are related to the same kind of site but for the different monomers of α7nAChr.

A7nAChr					
Desensitized		**Activated**		**Resting**	
Score (kcal/mol)	**Site**	**Score (kcal/mol)**	**Site**	**Score (kcal/mol)**	**Site**
-8.798	Site 1	-9.047	Site 3	-6.341	Site 3
-7.514	Site 1	-8.938	Site 3	-9.375	Site 1
-7.855	Site 1	-8.986	Site 3	-8.828	Site 1
-9.086	Site 3	-8.918	Site 3	-8.398	Site 1
-9.047	Site 3	-6.246	Site 1	-8.518	Site 1
-8.751	Site 3	-8.317	Site 3	-7.890	Site 2
-8.694	Site 3	-6.632	Site 1	-9.619	Site 2
-9.147	Site 3	-7.345	Site 1	-9.392	Site 2
-6.002	Site 2	-7.988	Site 1	-9.593	Site 2
-6.622	Site 2	-6.111	Site 1		
-6.594	Site 2	-10.581	Site 2		
-8.943	Site 2	-10.636	Site 2		
-7.996	Site 2				
-7.591	Site 1				
-8.798	Site 1				
-7.514	Site 4				

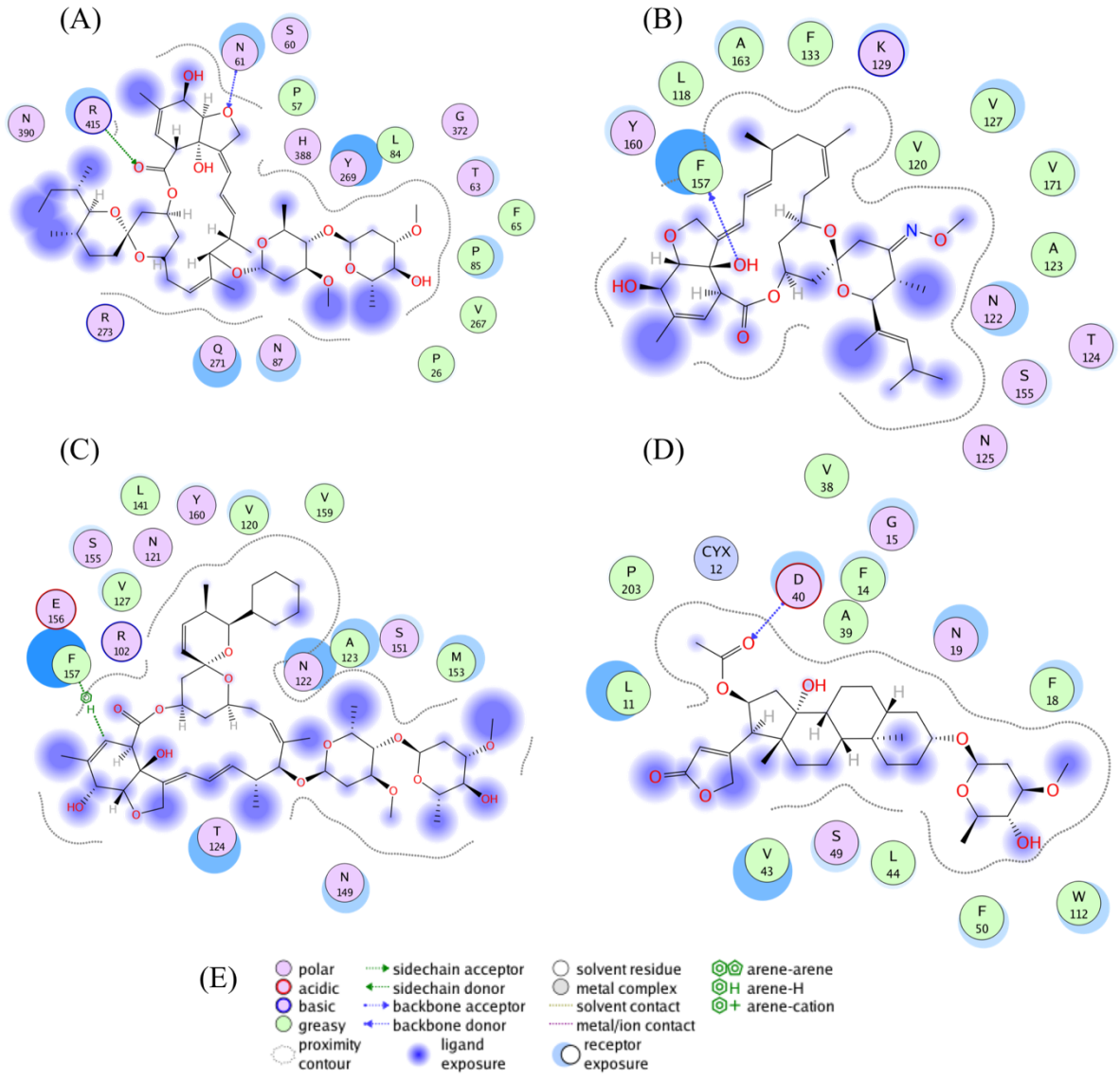

Figure S8. Ligand interaction plots of compounds selected for spike inhibition. (**A**) Ivermectin, (**B**) Moxidectin, (**C**) Doramectin (**D**) Oleandrin. A graphical key (**E**) is included to help interpret the 2-D part of the ligand interactions panel.

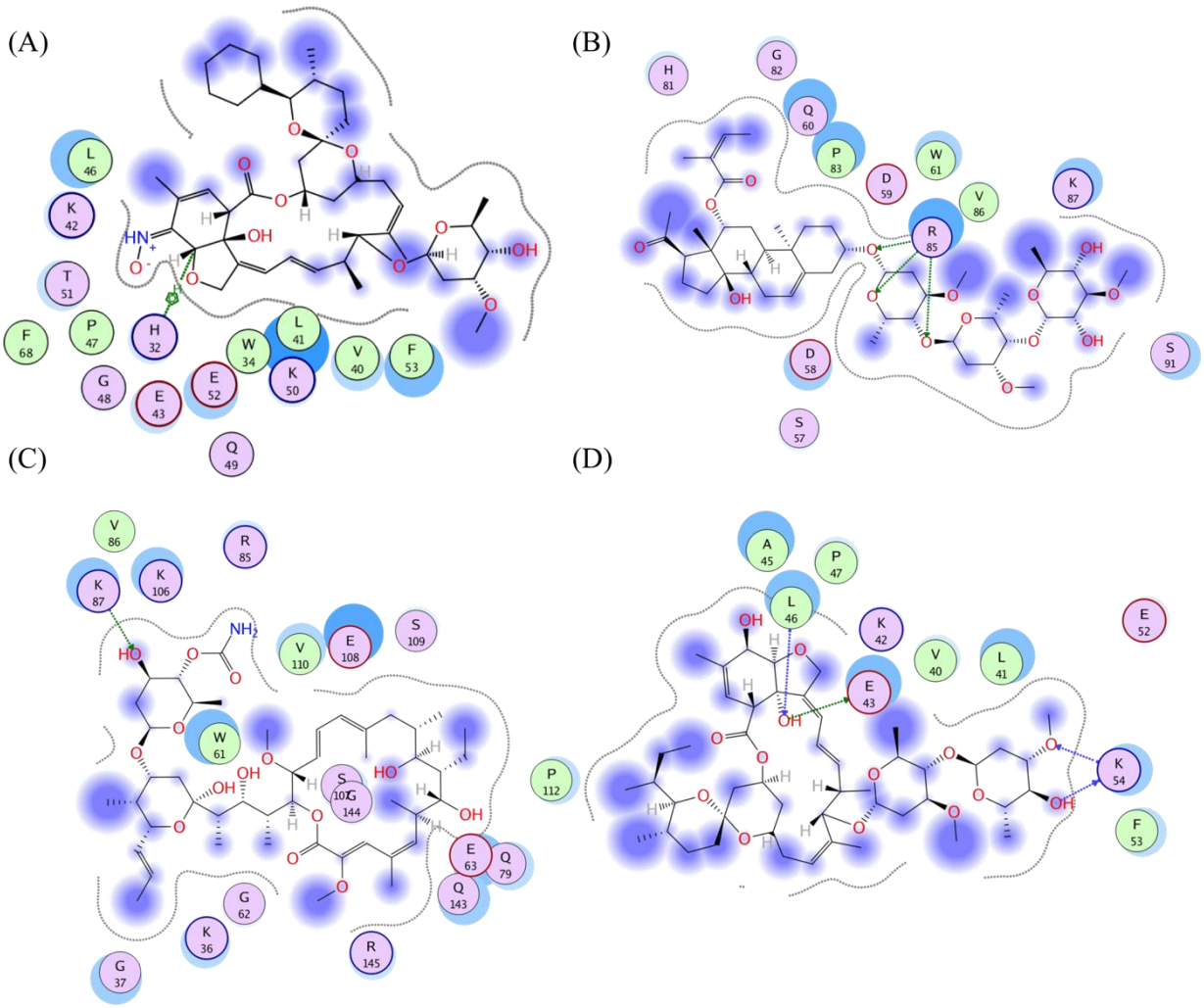

Figure S9. Ligand interaction plots of compounds selected for CD147 inhibition. (**A**) Selamectin, (**B**) P-57AS3, (**C**) Concanamycin_A and (**D**) Ivermectin. A graphical key is included in Figure S8(**E**).

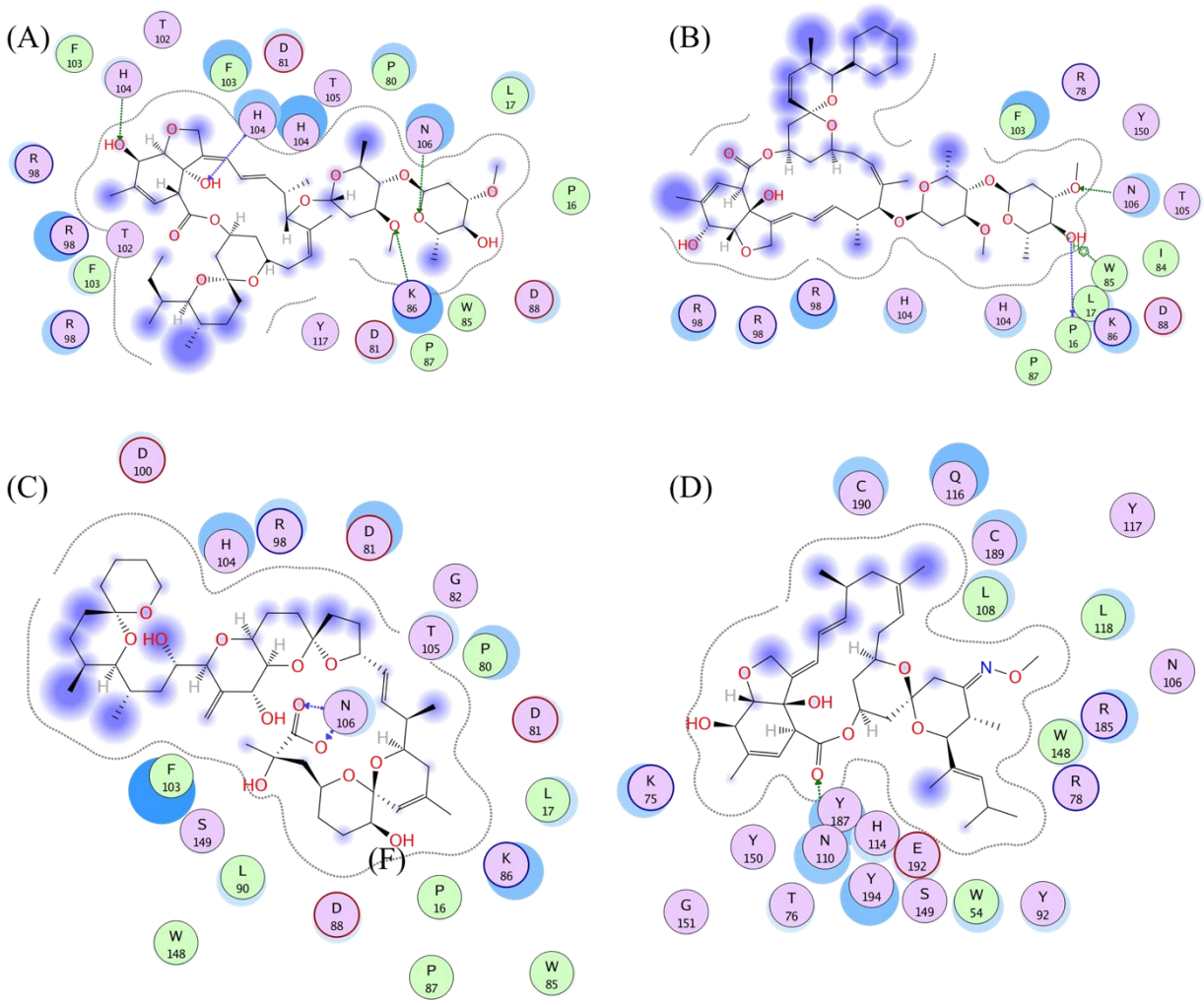

Figure S10. Ligand interaction plots of compounds selected for α7nAChr inhibition. (**A**) Ivermectin, (**B**) Doramectin , (**C**) Okadaic_acid, (**D**) Moxidectin. A graphical key is included in Figure S8(**E**).

Table S6. Amino acid mutations of SARS-CoV-2 Alpha, Beta, Gamma and Delta variants of SARS-CoV-2 with a focus on spike protein. (Reproduced from Aminpour et al. [3].) The domain to which each mutation belongs is indicated in parentheses.

B.1.1.7 (United Kingdom, Alpha)	**B.1.351 (South Africa, Beta)**	**P.1 (Brazil, Gamma)**	**B.1.617.2 (India, Delta)**
H69–V70 deletion (NTD)	L18F (NTD)	L18F (NTD)	T19R (NTD)
Y144 deletion (NTD)	D80A (NTD)	T20N (NTD)	157-158 Deletion (NTD)
N501Y (RBD)	D215G (NTD)	P26S (NTD)	L452 (RBD)
A570D	242-244 deletion (NTD)	D138Y (NTD)	T478(RBD)
P681H	R246I (NTD)	R190S (NTD)	D614G
T716I	K417N (RBD)	K417T (RBD)	P681R
S982A	E484K (RBD)	E484K (RBD)	D950N
D1118H	N501Y (RBD)	N501Y (RBD)	
	D614G	D614G	
	A701V	H655Y	
		T1027I	
		V1176F	

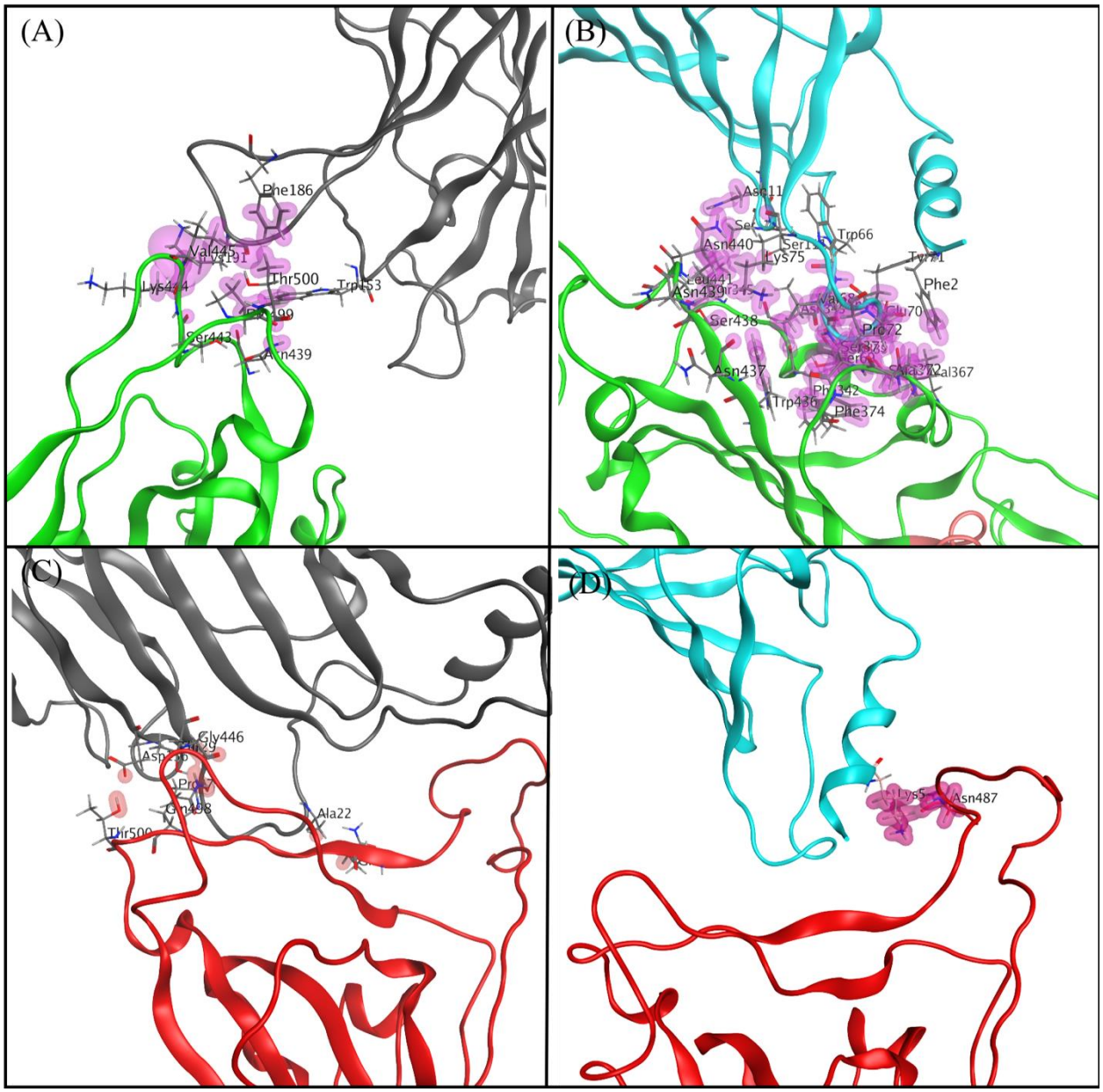

Figure S11. Protein-protein interaction between (**A**) chain E (gray) α7nAChr and chain C (green) of spike protein, (**B**) chain A (cyan) α7nAChr and chain C (green) of spike protein, (**C**) chain E (gray) α7nAChr and chain B (red) of spike protein, and (**D**) chain A (cyan) α7nAChr and chain B (red) of spike protein. For clarity, we didn't depict the VDW distance interactions in part (C) and (D).