Predicting binding models of N1H1 neuraminidase

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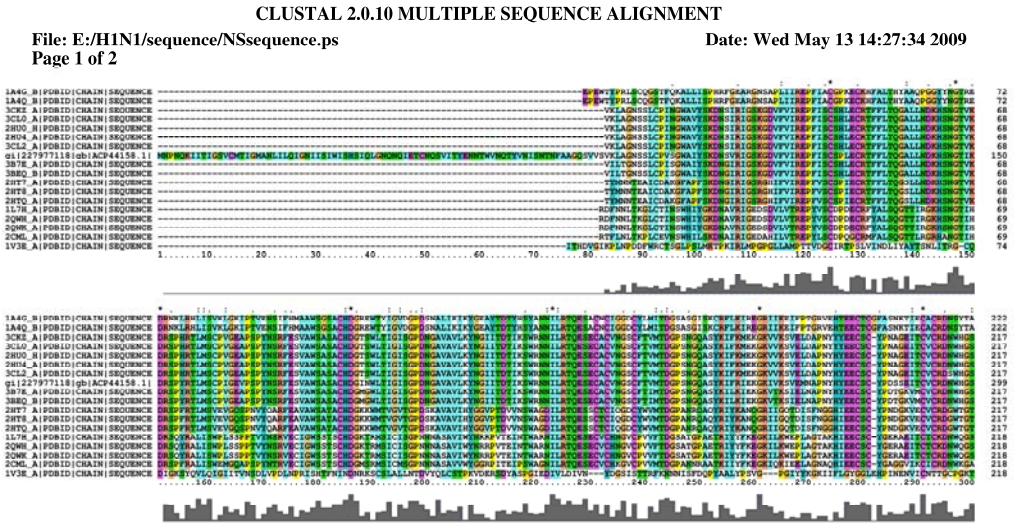
Computing resource of NCHC

機器群	機器名稱及其位址	備註
IBM Cluster 1350	irish2(140.110.122.62) irish3(140.110.122.63)	IBM Cluster 1350, 2048 CPUs
HP Superdome	Hermes(140.110.9.11)	SMP/ccNUMA, 64*2 CPU
HP Superdome 2	halen.nchc.org.tw (140.110.9.16)	SMP system with 88 processor cores and 1 tera byte memory 下載申請辦法
IBM P690	imp(140.110.13.2~140.110.13.3)	8 nodes(256cpus)
IBM P690A	ivan2(140.110.4.11)	3 nodes(96cpus)
SGI Origin 3800	scorpio(140.110.4.61)	SGI Origin3800, 48cpus
SGI Origin 2000	sophia (140.110.4.2)	SGI Origin2000, 32 cpus
SUNws	clio02 (140.110.9.5)	Sun Enterprise 10000,3 cpus
	Camelot (140.110.4.30)	Sun Ultra 60
SGI ws	sufi (140.110.4.17)	SGI Octane
	sarah (140.110.4.18)	
	schumna (140.110.4.19)	
DEC ws	duke01~08(140.110.4.41~48)	Compaq DS 20E
HP 64bit Cluster	triton1~triton192 (140.110.2.190)	HP rx2600 , 384CPUs「專用計算資源」以專案方式申請（每年受理二次，分別從一月份及八月份開始申請，下載申請辦法）。
Formosa II HPC Cluster	siraya.sro.nchc.org.tw(140.110.122.5)	IBM e326 320 CPU-Cores
AMD4P	amd4p.nchc.org.tw(140.110.17.5)	AMD Opteron(tm) Processor 844 1.8GHz x 4
AMD16P	amd16p.nchc.org.tw(140.110.17.76)	Dual-Core AMD Opteron (tm) Processor 8218 1.8GHz x 8
IBM P595	iliad.nchc.org.tw(140.110.13.30)	

Material of N1H1 neuraminidase (NS)

NS protein sequences:

>gi|227977118|gb|ACP44158.1| neuraminidase [Influenza A virus (A/California/04/2009(H1N1))]
MNPNQKIITIGSVCMTIGMANLILQIGNIISIWISHSIQLGNQNQIETCNQSVITYENNTWVNQ
TYVNISNTNFAAGQSVVSVKLAGNSSLCPVSGWAIYSKDNSVRIGSKGDVFVIREPFISCSPL
ECRTFFLTQGALLNDKHSNGTIKDRSPYRTLMSCPIGEVPSPYNSRFESVAWSASACHDGIN
WLTIGISGPDNGAVAVLKYNGIITDTIKSWRNNILRTQESECACVNGSCFTVMTDGPSNGQA
SYKIFRIEKGKIVKSVEMNAPNYHYEECSCYPDSSEITCVCRDNWHGSNRPWVSFNQNLEY
QIGYICSGIFGDNPRPNDKTGSCGPVSSNGANGVKGFSFKYGNGVWIGRTKSISSRNGFEMI
WDPNGWTGTDNNFSIKQDIVGINEWSGYSGSFVQHPELTGLDCIRPCFWVELIRGRPKENT
IWTSGSSISFCGVNSDTVGWSWPDGAELPFTIDK

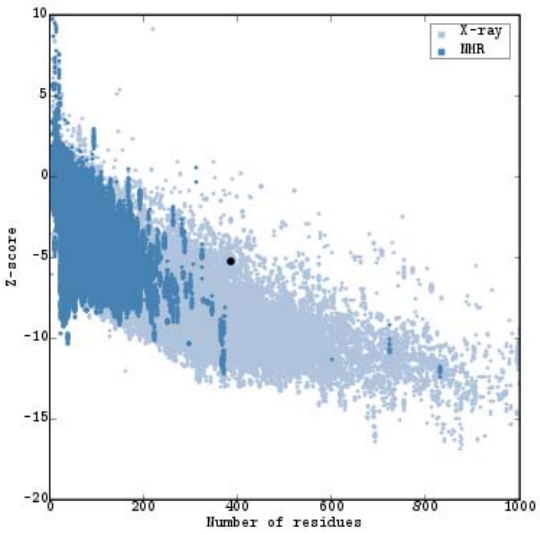


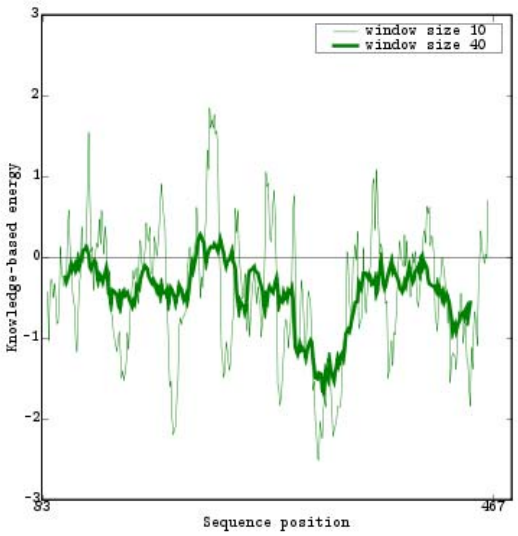
Because the modeller best template % seq id is equal to 88.831, we chose the pdb file named 3b7e as the template structure for homology modeling calculations.

Homology modeling of NS

The modeller and Amber molecular simulations softwares were applied to our homology modeling calculations. We also used the prosa and procheck methods to check the quality of our model. The results are shown below:

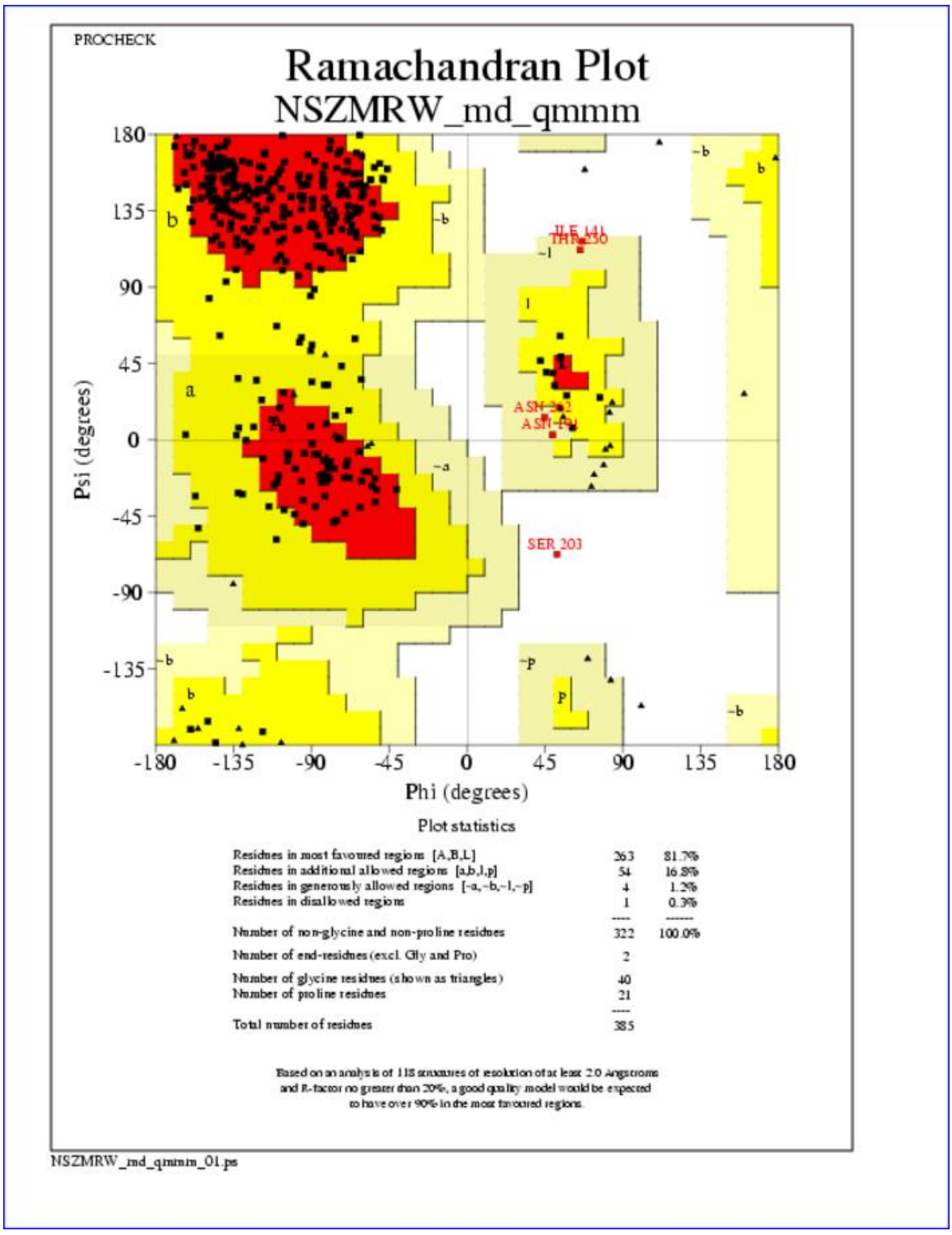
PROSA: z score = -5.22



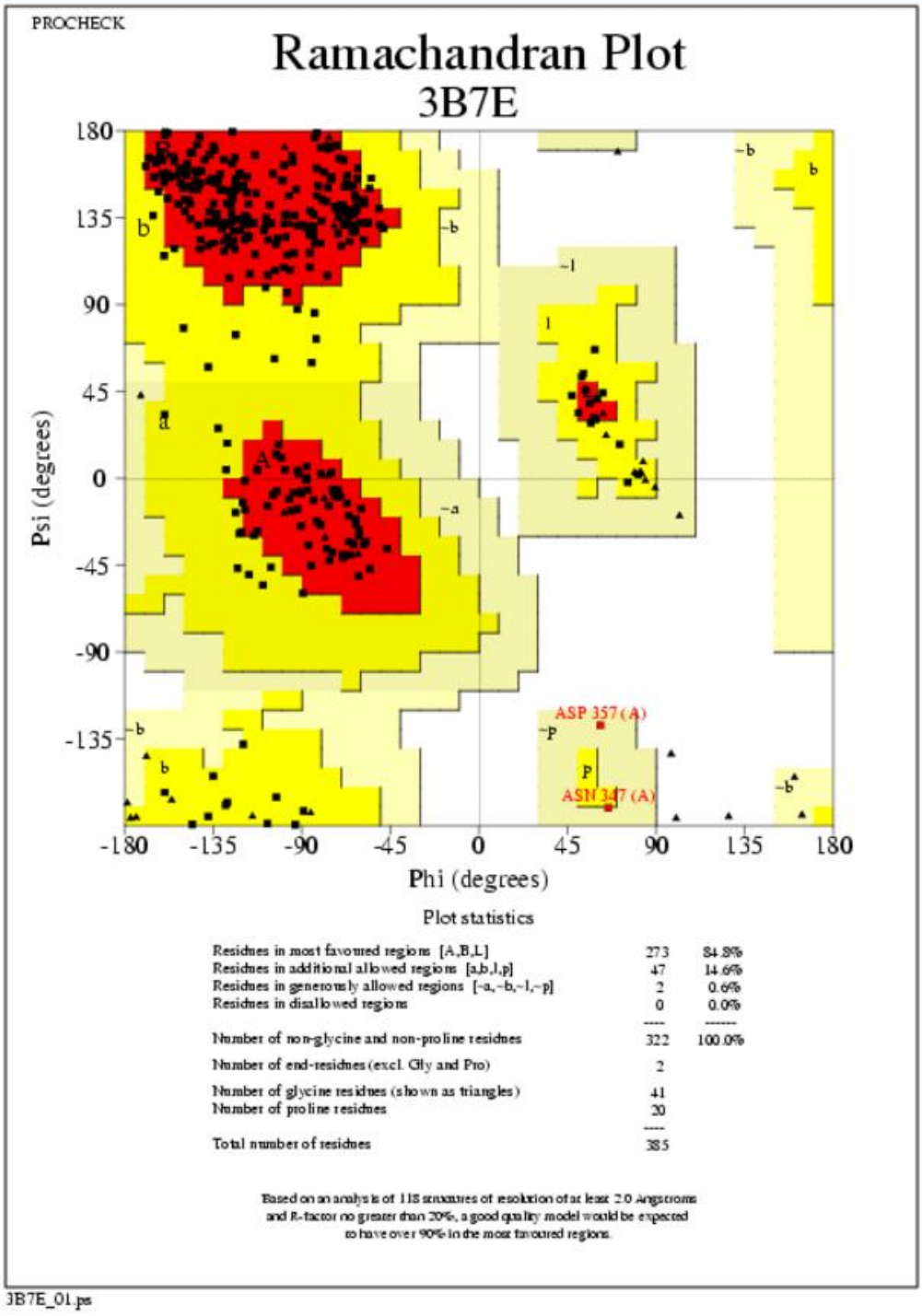


Procheck:

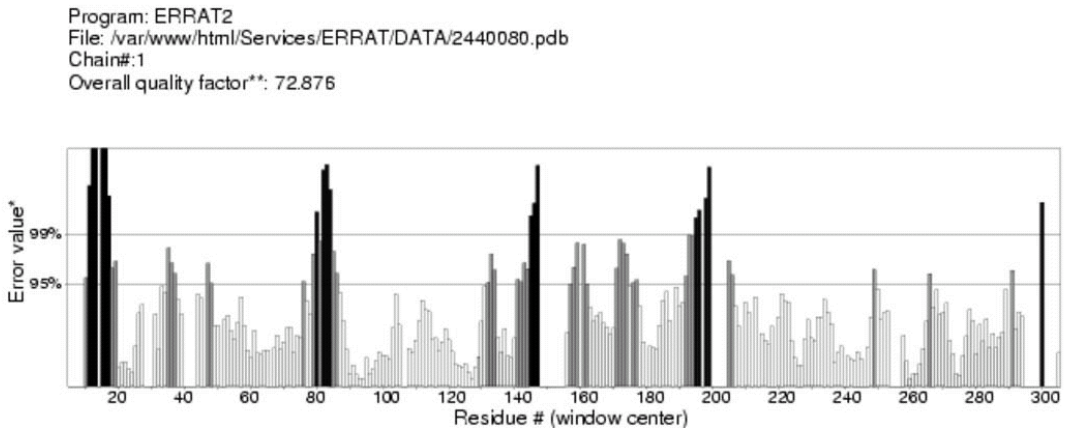
Our model



3B7E: A chain (template structure)



ERRAT2:

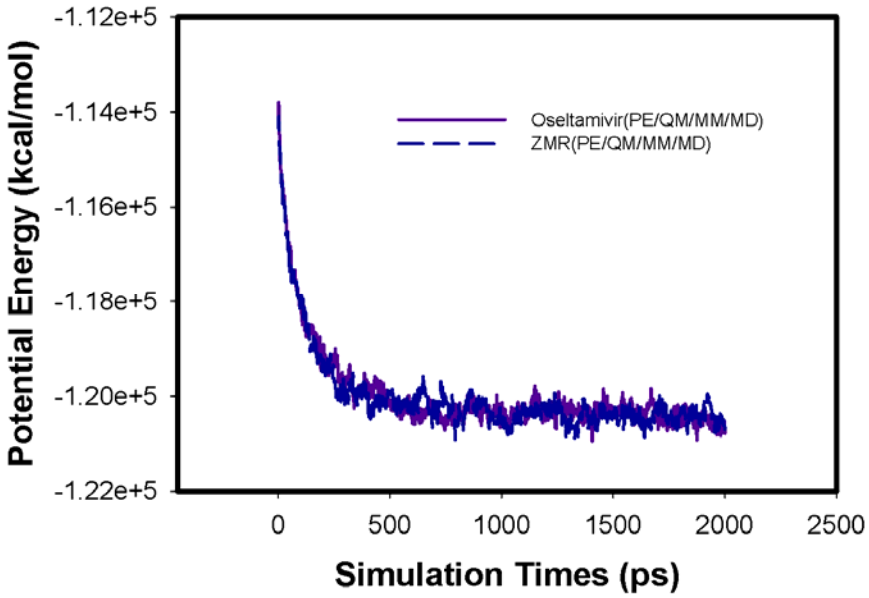


Summaries of our results were indicate that one residue (Ser203) of our NS model was located at the disallowed region of Ramachandran plot. Then, we checked the template structure (PDB ID: 3B7E) and found that two residues of the structures were located at the disallowed region of Ramachandran plot. And the ERRAT2 and PROSA scores are 72.875 and -5.22 respectively. So, we think our model may be suitable for the drug target of H1N1 virus treatments.

Docking Oseltamivir and Tamiflu (ZMR) compound into NS and MD simulations

The dock 6.2, Amber, and Gaussian 03 were applied to our calculations. The MD setting: 2 ns + Tip3 water. The results are shown below:

Potential energy:



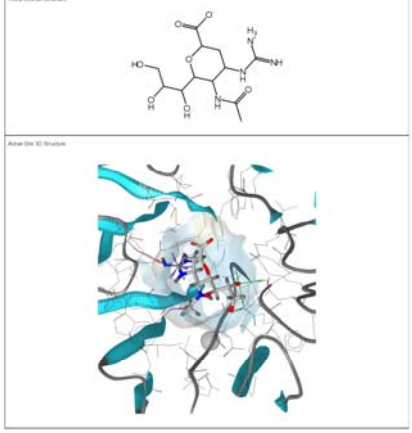
Dock score:

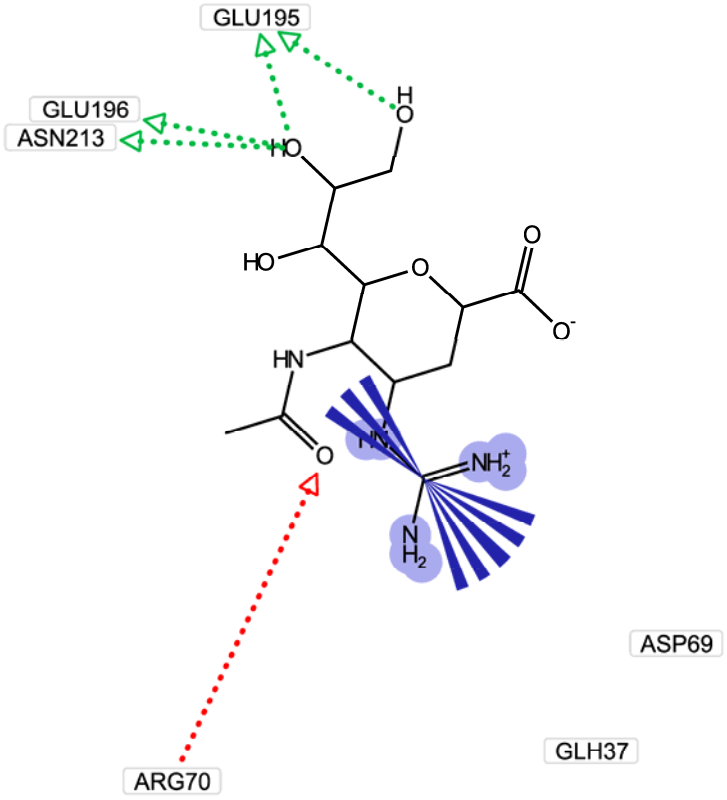
Compound	ZMR	Oseltamivir:
kcal/mol		
Elestostatic	0.279053	0
Van der Waals	-29.583820	-33.770145
Grid score	-29.304768	-33.770145

ZMR:

no complex id: ZMR386

PDB Ligand Key	ZMR386
PDB Complex ID	no complex id
Experimental Type & Resolution	default: X-Ray(not available A)
PDB Classification	not available
Ligand Name	n.a
Deposition Date	not available
Molecular Formula	C12 H22 N4 O7

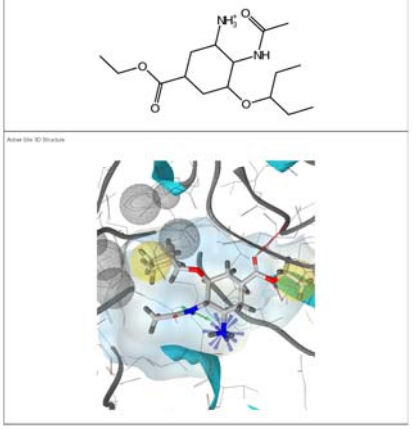


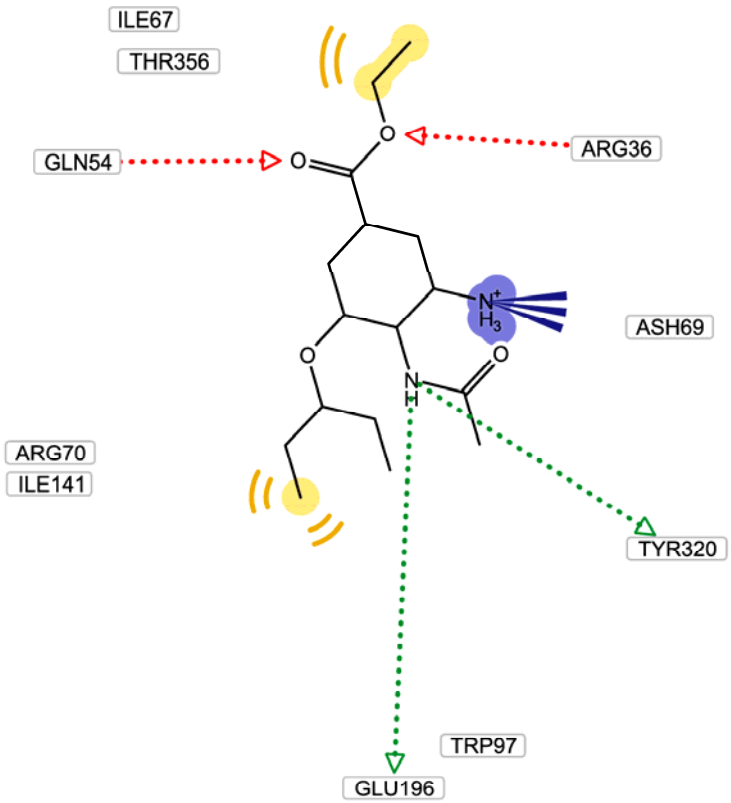


Oseltamivir:

no complex id: MOL386

PDB Ligand Key	MOL386
PDB Complex ID	no complex id
Experimental Type & Resolution	default: X-Ray(not available A)
PDB Classification	not available
Ligand Name	n.a
Deposition Date	not available
Molecular Formula	C16 H31 N2 O4





Summaries of binding mod

Compound	ZMR	Oseltamivir:
Residues		
Elestostatic	Asp69, Glu37	Asp69
Van der Waals	Null	Ile67, The356, Arg70, Ile141, Trp97
Hydrogen bonding	Arg70, Asn213,Glu196, Glu195	Gln54, Arg36, Tyr320, Glu196,

Summaries of our calculations indicated that the complex system (NS and two drugs) were tended to equilibrium after 500 ps. And the residues (Asp69 and Glu196) may play important roles in H1N1 virus treatments.

Screen of Chinese herb database

The dock6.2 software was applied in the docking calculations. The screening database is from the Chinese natural product database. After docking simulations, we found the dock scores of the compounds (~1000 herb compound) was great than the ones form the two drugs. And we also found the dock scores of the compounds (HR1039 and HR1040) were double of the ones form the two drugs. We put the target protein and 50 best selected Chinese herb compound.