

# Natural Products from Marine Actinomycete Genus *Salinispora* Might Inhibit 3CLpro and PLpro Proteins of SARS-CoV-2: An In Silico Evidence

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**Table S1.** List of natural products from genus *salinispora* involved in this work.

Salinispora Genus		
<i>S. arenicola</i>	<i>S. pacifica</i>	<i>S. tropica</i>
Arenamide A - C	Cyanosporaside A-F	Antiprotealide
Arenicolide A - C	Desferrioxamine E	Bromosalinosporamide
Arenimycin A - D	Enterocin	Desferrioxamine B
Cycloaspeptide A	Homoseongomycin	Lymphostin
Cyclomarin A, C	Lomaiviticin A-E	Salinosporamide A-J
Cyclomarazine A and B	Lymphostin	Sioxanthin
Ikarugamycin	Mycalamide A	Sporolide A and B
Lovastatin	Pacificanone A and B	Salinilactam
Neolymphostin A-D	Salinipyrone A and B	Salinipostin A-K
Retimycin A	Salinosporamide K	Salinichelin A-C
Salinaphthoquinone A-E	Salinipostin A-K	Sal-GBL1
Rifamycin B, O, S, SV,W	Salinichelin A-C	Sal-GBL2
27-O-demethylrifamycin SV	Tirandalydigin	
27-O-demethyl-25-O-desacetyl rifamycin SV		
N-(2'-phenylethyl)isobutyramide		
2-methyl-N-(2'-phenylethyl)butyramide		
N-(2'-phenylethyl)isovaleramide		
Saliniketal A and B		
Salinilactone A-H		
Saliniquinone A-F		
Salinisporamycin		
Staurosporine		
BE-43547A1		
BE-43547A2		
Isopimara-8,15-diene		
Isopimara-8,15-dien-19-ol		
N-(3-oxodecanoyl)-L-homoserine lactone		

N-(3-oxododecanoyl)-L-homoserine lactone  
 Salinipostin A-K  
 Salinichelin A-C  
 Rifsaliniketal  
 Neolymphostinol A-D  
 Lymphostinol  
 Emericellamide A and B

**Table S2:** Canonical SMILES for selected natural products

Top Ligands	Formulae	SMILES
Bromosalinosporamide	C <sub>15</sub> H <sub>20</sub> BrNO 4	<chem>CC12C(C(=O)NC1(C(=O)O2)C(C3CCCC=C3)O)CCBr</chem>
Cycloaspeptide A	C <sub>36</sub> H <sub>43</sub> N <sub>5</sub> O <sub>6</sub>	<chem>CC1C(=O)N(C(C(=O)NC(C(=O)N(C(C(=O)NC2=CC=CC=C2C(=O)N1)CC3=CC=C(C=C3)O)C)CC(C)C)CC4=CC=CC=C4)C</chem>
Lymphostin	C <sub>16</sub> H <sub>14</sub> N <sub>4</sub> O <sub>3</sub>	<chem>CC(=O)N=C1C=C(C2=NC=C3C2=C1NC(=C3)C(=O)C=COC)N</chem>
Neolymphostinol B	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub>	<chem>CCC(=O)NC1=CC(=N)C2=NC=C3C2=C1NC(=C3)C(=O)CCO</chem>
Rifamycin B	C <sub>39</sub> H <sub>49</sub> N <sub>14</sub> O <sub>14</sub>	<chem>CC1C=CC=C(C(=O)NC2=CC(=C3C(=C2O)C(=C(C4=C3C(=O)C(O4)(OC=CC(C(C(C(C(C(C1O)C)O)C)OC(=O)C)C)OC)C)O)OCC(=O)O)C</chem>
Salinaphthoquinone B	C <sub>18</sub> H <sub>15</sub> N <sub>5</sub> O <sub>5</sub>	<chem>CC1=CC(=C(OC1=O)C2=C(C(=CC3=C2C(=O)C=C(C3=O)N)C)O)C</chem>
Salinaphthoquinone E	C <sub>24</sub> H <sub>27</sub> N <sub>7</sub> O <sub>7</sub>	<chem>CC1C2C(C(OC1C(C(=O)O2)C)C(C)C(=O)C3=C(C(=CC4=C3C(=O)C=C(C4=O)N)C)O)C</chem>
Salinipostin A	C <sub>25</sub> H <sub>45</sub> O <sub>6</sub> P	<chem>CCCCCCCCCCCCCCCCOP1(=O)OCC2COC(=O)C2=C(O1)CCCC</chem>
Salinipostin C	C <sub>23</sub> H <sub>41</sub> O <sub>6</sub> P	<chem>CCCCCCCCCCCCCCCCOP1(=O)OCC2COC(=O)C2=C(O1)CCCC</chem>
Saliniquinone F	C <sub>23</sub> H <sub>18</sub> O <sub>6</sub>	<chem>Cc1cc2c(c3c1c(=O)cc(o3)[C@](C)(CC=C)O)C(=O)c4c(cccc4O)C2=O</chem>
Salinosporamide C	C <sub>14</sub> H <sub>18</sub> ClNO 3	<chem>CC1=C(C(=O)N2C1C(C3C2CC(=O)CC3)O)CCCl</chem>
Salinosporamide I	C <sub>16</sub> H <sub>22</sub> ClNO 4	<chem>CCC12C(C(=O)NC1(C(=O)O2)C(C3CCCC=C3)O)CCCl</chem>
Salinilactam	C <sub>28</sub> H <sub>39</sub> N <sub>5</sub> O <sub>5</sub>	<chem>CC1CC=CC=CC=C(C=CC=CC=CC(C(C(C(C=C=CC(=O)N1)C)O)O)O)C</chem>
Sporolide A	C <sub>24</sub> H <sub>23</sub> ClO <sub>1</sub> 2	<chem>CC1=C2C3(C4C(C1=O)(O4)C(C(=O)OCC(C5=C(C6=C(C=C5)C(C7(C6(O3)C(CC7O)O)O2)O)Cl)O)OC)O</chem>

**Table S3:** 3CL<sup>pro</sup> docking results and residue interactions category 1

Ligands	Binding affinity ('-4.0 to -5.9)	Interacting amino acids
Antiprotealide	-5.6	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Cyclomarin D	-5.8	THR24 THR25 THR26 LEU27 HIS41 SER46 MET49 TYR54 ASN142 GLY143 SER144 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189
Lomaiviticin A	-5.8	THR24 THR25 HIS41 VAL42 CYS44 SER46 MET49 TYR54 PHE140 LEU141 ASN142 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 GLN192
N-(3-Oxodecanoyl)-L-homoserine lactone	-5.2	HIS41 MET49 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
N-(3-oxododecanoyl)-L-homoserine lactone	-5.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
N-(2'-phenylethyl)isobutyramide	-5.5	HIS41 CYS44 ASP48 MET49 TYR54 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 GLN192
N-(2'-phenylethyl)isovaleramide	-5	HIS41 CYS44 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 GLN192
2-methyl-N-(2'-phenylethyl)butyramide	-5.9	HIS41 CYS44 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 GLN192
Retimycin A	-5	HIS41 MET49 TYR54 PHE140 LEU141 ASN142 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Rifamycin B	-5.9	LEU141 ASN142 GLY143 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 GLY170 ARG188 GLN189 THR190 GLN192
Rifamycin SW	-5.5	HIS41 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Sal-GBL1	-5.9	HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 CYS145 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 THR190 GLN192

Sal-GBL2	-5.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 GLN192
Salinilactone A	-5.1	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinilactone B	-4.9	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
Salinilactone C	-5.1	HIS41 CYS44 ASP48 MET49 TYR54 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
Salinilactone D	-4.7	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 ASP187 ARG188 GLN189
Salinilactone E	-5.1	HIS41 CYS44 ASP48 MET49 TYR54 HIS164 MET165 ASP187 ARG188 GLN189
Salinilactone F	-4.9	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 ASP187 ARG188 GLN189
Salinilactone G	-5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
Salinilactone H	-5.3	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin A	-5.1	THR25 HIS41 CYS44 MET49 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190
Salinipostin B	-5.3	THR25 THR26 LEU27 HIS41 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin C	-5.6	THR25 LEU27 HIS41 CYS44 THR45 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinipostin D	-5.6	THR25 HIS41 CYS44 MET49 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinipostin F	-5.6	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin G	-5.6	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin H	-5.8	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin I	-5.6	THR24 THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189

Salinipostin J	-5.5	THR25 HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinipostin K	-5.9	THR25 HIS41 CYS44 ASP48 MET49 TYR54 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192

**Table S4:** 3CL<sup>pro</sup> docking results and residue interactions category 2 (lower-moderate values)

Ligands	Binding affinity ('-6 to '- 6.9)	Interacting amino acids
Arenamide C	-6.9	THR24 THR25 THR26 LEU27 HIS41 MET49 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Arenicolide A	-6.4	THR24 THR25 HIS41 CYS44 THR45 SER46 MET49 TYR54 PHE140 LEU141 ASN142 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Arenicolide B	-6.9	THR25 HIS41 CYS44 MET49 TYR54 LEU141 ASN142 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Arenimycin B	-6.9	THR24 THR25 THR26 HIS41 CYS44 THR45 SER46 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 GLN192
Bromosalinosporamide	-6.1	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 PRO168 ASP187 ARG188 GLN189
Cyclomarazine A	-6.3	HIS41 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Cyclomarin A	-6.5	THR25 THR26 LEU27 HIS41 CYS44 SER46 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Cyclomarin C	-6.5	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 GLN192
Desferrioxamine B	-6.2	THR25 THR26 LEU27 HIS41 CYS44 THR45 ASP48 MET49 PRO52 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Emericellamide A	-6.9	THR24 THR25 THR26 LEU27 HIS41 CYS44 THR45 SER46 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 ARG188 GLN189 THR190 GLN192

Isopimara-8,15-dien-19-ol	-6.6	HIS41 CYS44 ASP48 MET49 TYR54 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Isopimara-8,15-diene	-6.9	HIS41 CYS44 MET49 TYR54 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Lomaiviticin C	-6.6	THR24 THR25 HIS41 CYS44 THR45 SER46 MET49 TYR54 LEU141 ASN142 MET165 GLU166 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Lomaiviticin E	-6	THR24 THR25 THR26 THR45 SER46 GLU47 MET49 LEU50 LEU141 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192
Mycalamide A	-6.5	THR25 LEU27 HIS41 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192
Pacificanone A	-6.8	THR25 THR26 LEU27 HIS41 MET49 TYR54 ASN142 GLY143 SER144 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Pacificanone B	-6.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189
Salinaphthoquinone A	-6.6	THR25 HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinichelin C	-6.7	THR25 THR26 LEU27 HIS41 VAL42 CYS44 THR45 ASP48 MET49 LEU50 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 HIS172 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Saliniketal B	-6.7	HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Salinipostin E	-6	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinipyronone A	-6.3	THR25 HIS41 VAL42 CYS44 ASP48 MET49 PRO52 TYR54 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinipyronone B	-6.6	HIS41 CYS44 ASP48 MET49 LEU50 TYR54 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192 ALA193
Salinosporamide A	-6.6	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189

Salinosporamide B	-6.8	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189
Salinosporamide C	-6.3	THR25 HIS41 CYS44 MET49 ASN142 CYS145 HIS164 MET165 ASP187 ARG188 GLN189
Salinosporamide E	-6.7	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 ASP187 ARG188 GLN189
Salinosporamide F	-6.1	HIS41 ASP48 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinosporamide G	-6.4	HIS41 MET49 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinosporamide H	-6.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 LEU141 ASN142 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinosporamide I	-6.5	THR25 HIS41 CYS44 MET49 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 GLN192
Salinosporamide J	-6.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Salinosporamide K	-6.2	HIS41 CYS44 ASP48 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189

**TableS5:** 3CL<sup>pro</sup> docking results and residue interactions category 2 (upper-moderate values)

Ligands	Binding affinity ('-7 to '- 7.9)	Interacting amino acids
Arenamide A	-7.5	THR24 THR25 THR26 HIS41 CYS44 ASP48 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Arenicolide C	-7.1	HIS41 MET49 PHE140 LEU141 ASN142 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192
BE-43547A1	-7	THR25 THR26 LEU27 HIS41 CYS44 ASP48 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
BE-43547A2	-7	THR25 THR26 LEU27 HIS41 CYS44 ASP48 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192

Cyanosporaside A	-7.5	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Cyanosporaside B	-7.7	THR25 THR26 LEU27 HIS41 VAL42 CYS44 MET49 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Cyanosporaside C	-7.6	THR24 THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
Cyanosporaside D	-7.2	THR25 HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Cyanosporaside E	-7.1	THR25 HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Cyclomarazine B	-7.1	THR24 THR25 HIS41 CYS44 THR45 SER46 ASP48 MET49 TYR54 ASN142 GLY143 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
Emericellamide B	-7.5	THR25 HIS41 CYS44 ASP48 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Enterocin	-7.7	THR25 HIS41 CYS44 ASP48 MET49 TYR54 PHE140 LEU141 ASN142 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 HIS172 ASP187 ARG188 GLN189
Homoseongomycin	-7.8	THR25 HIS41 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Lomaiviticin B	-7.1	HIS41 CYS44 MET49 TYR54 LEU141 ASN142 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Lomaiviticin D	-7.3	THR24 THR25 THR26 HIS41 VAL42 CYS44 SER46 MET49 LEU50 TYR54 PHE140 LEU141 ASN142 GLY143 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Lymphostin	-7.6	THR25 THR26 LEU27 HIS41 CYS44 MET49 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166
Lymphostinol	-7.6	HIS41 CYS44 ASP48 MET49 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 GLN192
Neolymphostin A	-7.7	HIS41 CYS44 ASP48 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Neolymphostin B	-7.9	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 VAL186 ASP187 ARG188 GLN189 THR190 GLN192



Neolymphostin C	-7.3	THR25 THR26 LEU27 HIS41 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Neolymphostinol A	-7.4	HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 LEU141 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 GLN192
Neolymphostinol B	-7.7	HIS41 CYS44 MET49 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 THR190 GLN192
Neolymphostinol C	-7.5	HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 LEU141 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 GLN192
Neolymphostinol D	-7.6	THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Rifamycin S	-7.9	THR24 THR25 THR26 HIS41 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Rifamycin W	-7.5	THR25 HIS41 CYS44 ASP48 MET49 PRO52 TYR54 ASN142 GLY143 CYS145 MET165 GLU166 LEU167 PRO168 THR169 GLY170 VAL186 ASP187 ARG188 GLN189 GLN192
Salinaphthoquinone E	-7.6	HIS41 MET49 ASN142 GLY143 CYS145 HIS163 MET165 GLU166 ARG188 GLN189
Salinichelin A	-7.7	THR24 THR25 THR26 LEU27 HIS41 SER46 MET49 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 HIS172 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinichelin B	-7.1	THR25 THR26 LEU27 HIS41 MET49 TYR54 TYR118 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 HIS172 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Saliniketal A	-7	HIS41 MET49 TYR54 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinilactam	-7.5	HIS41 MET49 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Saliniquinone E	-7.8	THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 LEU141 ASN142 CYS145 MET165 GLU166 ASP187 ARG188 GLN189
Salinosporamide D	-7	HIS41 CYS44 ASP48 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 VAL186 ASP187 ARG188 GLN189
Sporolide A	-7	THR24 THR25 HIS41 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 ASP187 ARG188 GLN189
Sporolide B	-7.3	THR24 THR25 HIS41 CYS44 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Staurosporine	-7.6	HIS41 MET49 ASN142 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192

Sioxanthin	-7.2	ARG40 GLU55 MET82 GLN83 ASN84 CYS85 ARG105 PRO132 ASN133 PHE134 GLY179 ASN180 PHE181 TYR182 GLY183 PRO184 PHE185 VAL186 GLY195 THR196 ASP197 THR198 ASN238 GLU240 PRO241
Tirandalydigin	-7.5	THR24 THR25 HIS41 VAL42 CYS44 THR45 SER46 ASP48 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 ASP187 ARG188 GLN189 GLN192
27-O-demethylrifamycin SV	-7.8	THR24 THR25 THR26 LEU27 HIS41 SER46 MET49 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ARG188 GLN189 GLN192

**Table S6:** 3CL<sup>pro</sup> docking results and residue interactions (category 3)

Ligands	Binding affinity ('-8.0 and higher)	Interacting amino acids
Arenamide B	-8.2	THR25 HIS41 CYS44 THR45 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 THR169 GLY170 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Arenimycin A	-8.5	THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 THR169 GLY170 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Arenimycin C	-8.5	THR24 THR25 THR26 LEU27 HIS41 MET49 TYR118 ASN119 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192
Arenimycin D	-8.7	THR25 THR26 LEU27 HIS41 CYS44 MET49 TYR54 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 GLY170 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Cyanosporaside F	-8.2	THR25 THR26 HIS41 CYS44 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 HIS172 ASP187 ARG188 GLN189 THR190 GLN192
CycloaspeptideA	-8.5	HIS41 CYS44 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 PRO168 HIS172 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Desferrioxamine E	-8.5	HIS41 MET49 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ARG188 GLN189 THR190 ALA191 GLN192
Ikarugamycin	-9	THR25 HIS41 VAL42 CYS44 MET49 ASN142 GLY143 CYS145 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192

Lovastatin	-8	THR25 THR26 LEU27 HIS41 CYS44 ASP48 MET49 LEU50 PRO52 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Neolymphostin D	-8.2	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 GLN192
Rifsaliniketal	-8.5	THR25 HIS41 CYS44 ASP48 MET49 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR190 GLN192
Rifamycin O	-8	THR25 LEU27 HIS41 VAL42 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 ALA191 GLN192
Salinaphthoquinone B	-8.2	HIS41 MET49 ASN142 GLY143 CYS145 HIS163 MET165 GLU166 LEU167 PRO168 ASP187 ARG188 GLN189 THR 190 GLN 192
Salinaphthoquinone C	-8	HIS41 CYS44 ASP48 MET49 LEU50 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinaphthoquinone D	-8.2	THR25 HIS41 MET49 TYR54 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 ASP187 ARG188 GLN189
Saliniquinone A	-8	THR24 THR25 THR26 LEU27 HIS41 CYS44 MET49 LEU50 TYR54 ASN142 GLY143 CYS145 GLU166 ASP187 ARG188 GLN189
Saliniquinone B	-8	THR25 THR26 LEU27 HIS41 CYS44 ASP48 MET49 LEU50 TYR54 ASN142 GLY143 CYS145 GLU166 ASP187 ARG188 GLN189
Saliniquinone C	-8.2	HIS41 CYS44 ASP48 MET49 PRO52 TYR54 LEU141 ASN142 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Saliniquinone D	-8	THR25 THR26 LEU27 HIS41 CYS44 MET49 LEU50 TYR54 ASN142 GLY143 CYS145 MET165 GLU166 ASP187 ARG188 GLN189
Saliniquinone F	-8.2	HIS41 CYS44 MET49 TYR54 ASN142 CYS145 HIS164 MET165 GLU166 PRO168 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
Salinisporamycin	-8.2	THR24 THR25 THR26 LEU27 HIS41 VAL42 CYS44 MET49 ASN142 GLY143 CYS145 HIS164 MET165 GLU166 LEU167 PRO168 ARG188 GLN189 THR190 GLN192
27-O-demethyl-25-O-desacetyl rifamycin SV	-8.5	THR24 THR25 THR26 HIS41 CYS44 SER46 MET49 LEU141 ASN142 GLY143 SER144 CYS145 HIS163 HIS164 MET165 GLU166 GLN189

**Table S7:** PL<sup>pro</sup> docking results and residue interactions (category 1)

Ligands	Binding affinity ('-4.0 to -5.9)	Interacting amino acids
Antiprotealide	-5.5	ASP164 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Arenamide C	-4.8	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 THR265 GLY266 GLN269 CYS270 GLY271 HIS272
Arenicolide B	-5.7	ASP164 ARG166 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 CYS270 TYR273 THR301
Arenimycin B	-5.9	ASP164 ARG166 MET208 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 PRO299 THR301
Bromosalinosporamide	-5.5	PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 PRO299
Cyanosporaside A	-5.1	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 THR265 GLY266 GLN269 CYS270 GLY271 HIS272
Cyanosporaside C	-5.7	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 THR265 GLN269 CYS270 GLY271 HIS272 ASP286 ASP164 PRO248 ALA249 GLN250 TYR264 GLY266 ASN267 TYR268 PRO299
Cyanosporaside D	-5	LEU162 GLY163 ASP164 VAL165 ARG166 GLU167 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Cyclomarin A	-4.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274
Cyclomarin C	-5.2	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274 ASP286
Cyclomarin D	-4.7	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 GLU263 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286 LEU289
Emericellamide A	-5.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 THR265 CYS270 GLY271 HIS272
Enterocin	-5.9	TRP106 ASN109 CYS111 LEU162 THR265 GLY266 GLN269 CYS270 GLY271 HIS272 TYR273 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 PRO299
Isopimara-8,15-diene	-5.5	ASP164 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Lomaiviticin A	-5.2	TRP106 ASN109 LEU162 GLN250 GLU263 THR265 CYS270 GLY271 HIS272 LYS274 CYS284 ASP286 TYR296 LYS297
Lomaiviticin B	-4.5	ASN109 CYS111 LEU162 GLU263 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286

Lomaiviticin C	-4.8	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274
Lomaiviticin D	-5	TRP106 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 CYS270 HIS272 LYS274 ASP286 PRO299
Lomaiviticin E	-5.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 GLU161 LEU162 GLY163 TYR264 THR265 ASN267 GLN269 CYS270 GLY271 HIS272 TYR273 LYS274
Mycalamide A	-5.1	TYR112 GLY163 ASP164 VAL165 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Pacifcanone A	-5.7	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Rifamycin SV	-5.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 ASN267 CYS270 GLY271 HIS272 ASP286
Rifamycin W	-5.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274
Salinilactam	-5.6	TRP106 ASN109 LEU162 THR265 GLY266 CYS270 GLY271 HIS272 LYS274 ASP286
Salinilactone A	-5.9	LEU162 GLY163 ASP164 VAL165 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinilactone B	-5.9	LEU162 GLY163 ASP164 VAL165 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinilactone D	-5.5	ASP164 VAL165 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinilactone E	-5.7	ASP164 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Salinilactone F	-5.7	GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 TYR273 THR301
Salinilactone G	-5.9	LEU162 GLY163 ASP164 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinipostin C	-5.9	TRP106 ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 TYR264 THR265 CYS270 GLY271 HIS272 TYR273 LYS274
Salinipostin D	-5.9	CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Salinipostin F	-5.9	LYS157 GLU161 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 CYS270 TYR273 THR301
Salinipostin G	-5.5	GLY163 ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 TYR273 PRO299 THR301

Salinipostin H	-5.9	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 TYR273 THR301
Salinipostin I	-5.9	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 CYS270 TYR273 PRO299 THR301
Salinipostin K	-5.9	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 ASP164 PRO248 TYR264 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Salinosporamide C	-5.8	ASP164 ARG166 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Salinosporamide E	-4.9	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 GLN269 CYS270 GLY271 HIS272 TYR273
Salinosporamide F	-5.9	LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinosporamide I	-5.7	LEU162 GLY163 ASP164 VAL165 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 GLY271 TYR273 THR301 ASP302
Sporolide A	-4.8	TRP106 ASN109 CYS111 LEU162 CYS270 GLY271 HIS272
Sporolide B	-4.4	ASN109 GLY160 LEU162 TYR268 GLN269 CYS270 GLY271 HIS272
Sioxanthin	-4.9	HIS73 THR74 ASP76 SER78 PHE79 ARG82 ALA153 TYR154 ASN156 ASP164 ARG166 GLU167 SER170 TYR171 GLN174 HIS175 MET206 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 THR301
27-O-demethylrifamycin SV	-5.2	TRP106 ASN109 CYS111 LEU162 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272
27-O-demethyl-25-O-desacetyl- rifamycin SV	-5.5	TRP106 ASN109 CYS111 LEU162 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274 ASP286

**Table S8:** PL<sup>pro</sup> docking results and residue interactions category 2 (lower-moderate values)

Ligands	Binding affinity ( <sup>-6.0 to -6.9</sup> )	Interacting amino acids
Arenamide A	-6.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 TYR264 THR265 GLY266 ASN267 GLN269 CYS270 GLY271_HIS272 LYS274
Arenamide B	-6.8	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 GLY163 TYR264 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274
Arenicolide A	-6.1	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Arenicolide C	-6.9	LEU162 GLY163 ASP164 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 TYR273 THR301
Arenimycin A	-6.7	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 GLN269 CYS270 GLY271 HIS272 LYS274 ASP286 LEU289 THR291
Arenimycin C	-6	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 THR265 CYS270 GLY271 HIS272 LYS274 CYS284 ILE285 ASP286 LEU289 THR291
BE-43547A1	-6.5	TRP106 ASN109 ASN110 CYS111 LEU162 GLY163 ASP164 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 LYS274 ASP286
BE-43547A2	-6.2	LEU162 GLY163 ASP164 VAL165 PRO247 PRO248 ALA249 GLN250 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 PRO299
Cyanosporaside B	-6.1	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 GLY163 GLN269 CYS270 GLY271 HIS272
Cyanosporaside E	-6.5	ASP164 ARG166 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273
Cyanosporaside F	-6.5	ASN109 CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
CycloaspeptideA	-6	TRP106 ALA107 ASP108 ASN109 CYS111 TYR112 LEU162 GLY163 TYR264 CYS270 GLY271 HIS272 TYR273 ASP286
Cyclomarazine A	-6.5	ASP164 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 TYR273 THR301 LYS157 LEU162 GLY163 ARG166
Desferrioxamine B	-6.9	LYS157 GLU161 LEU162 GLY163 ASP164 VAL165 ARG166 GLU167 MET208 SER245 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 PRO299 THR301 ASP302
Desferrioxamine E	-6.2	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 VAL159 GLY160 LEU162 GLN269 CYS270 GLY271 HIS272

Emericellamide B	-6.1	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 LEU162 ASP164 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 ASP286 TYR273 PRO299 THR301
Isopimara-8,15-dien-19-ol	-6.5	GLY163 ASP164 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Lovastatin	-6.5	GLY163 ASP164 VAL165 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301 ASP302
N-(3-Oxodecanoyl)-L-homoserine lactone	-6.5	ASN109 CYS111 TYR112 LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
N-(3-oxododecanoyl)-L-homoserine lactone	-6.7	ASN109 CYS111 TYR112 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
N-(2'-phenylethyl)isobutyramide	-6.9	ASN109 CYS111 TYR112 LEU162 GLY163 ASP164 VAL165 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
N-(2'-phenylethyl)isovaleramide	-6.2	LYS157 LEU162 GLY163 ASP164 VAL165 GLU167 PRO247 PRO248 TYR264 TYR268 GLN269 GLY271 TYR273 THR301
2-methyl-N-(2'-phenylethyl)butyramide	-6.7	LEU162 GLY163 ASP164 VAL165 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Pacificanone B	-6.5	ASN109 CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 GLU167 TYR264 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273
Rifsaliniketal	-6.9	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 CYS270 TYR273 PRO299 THR301
Rifamycin B	-6	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 THR265 GLN269 CYS270 GLY271 HIS272 LYS274 ASP286
Rifamycin O	-6.5	TRP106 ALA107 ASP108 ASN109 ASN110 GLU263 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286
Rifamycin S	-6.1	TRP106 ASN109 LEU162 GLU263 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286
Sal-GBL1	-6.1	TYR112 LEU162 GLY163 ASP164 VAL165 GLU167 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Sal-GBL2	-6	LEU162 GLY163 ASP164 GLU167 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 CYS270 GLY271 TYR273 THR301 ASP302
Salinaphthoquinone A	-6.5	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 TYR264 TYR268 GLN269 CYS270 GLY271 TYR273
Salinaphthoquinone B	-6.5	TRP106 ALA107 ASN109 ASN110 CYS111 LEU162 GLY163 CYS270 GLY271 HIS272



Salinaphthoquinone C	-6.7	GLY163 ASP164 VAL165 ARG166 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinaphthoquinone E	-6.9	PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 CYS270 PRO299
Salinichelin A	-6.5	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 GLY160 LEU162 GLY163 ASP164 GLU263 TYR264 THR265 GLN269 CYS270 GLY271 HIS272 TYR273 LYS274
Salinichelin B	-6.5	LYS157, LEU162 GLY163 ASP164 VAL165 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 PRO299 THR301
Salinichelin C	-6.5	TYR112 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 PRO299 THR301
Saliniketal A	-6.9	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 TYR273 PRO299 THR301
Saliniketal B	-6.9	GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 TYR273 PRO299 THR301
Salinilactone C	-6.1	LEU162 GLY163 ASP164 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Salinilactone H	-6.6	LEU162 GLY163 ASP164 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 GLY271 TYR273 THR301 ASP302
Salinipostin A	-6	ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Salinipostin B	-6.1	TRP106 ASN109 CYS111 TYR112 LEU162 GLY163 ASP164 PRO248 TYR264 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Salinipostin E	-6	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 ASP164 PRO248 TYR264 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Salinipostin J	-6.7	ASN109 CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Saliniquinone A	-6.9	TRP106 ASN109 CYS111 LEU162 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286
Salinosporamide A	-6.5	LYS157 LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301 ASP302

Salinosporamide D	-6.5	LEU162 GLY163 ASP164 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinosporamide G	-6.5	LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinosporamide H	-6.1	LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Salinosporamide J	-6.5	LYS157 LEU162 GLY163 ASP164 ARG166 MET208 SER245 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301 ASP302

**Table S9:** PL<sup>pro</sup> docking results and residue interactions category 2 (upper-moderate values)

Ligands	Binding affinity ( <sup>-</sup> 7.0 to <sup>-</sup> 7.9)	Interacting amino acids
Arenimycin D	-7.7	ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 THR301
Cyclomarazine B	-7.9	ASP164 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 TYR273 PRO299 THR301 HIS272
Ikarugamycin	-7.2	ASP164 ARG166 MET208 PRO247 PRO248 ALA249 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273 THR301
Lymphostin	-7.6	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 TYR268 GLN269 TYR273 THR301
Lymphostinol	-7.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 ALA246 PRO248 TYR264 TYR268 GLN269 TYR273 THR301 ASP302
Retimycin A	-7.7	TRP106 ASN109 CYS111 LEU162 TYR264 THR265 GLY266 ASN267 GLN269 CYS270 GLY271 HIS272 LYS274
Salinipyrone A	-7	LYS157 LEU162 GLY163 ASP164 VAL165 GLU167 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 TYR273
Salinipyrone B	-7.5	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 SER245 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 GLY271 TYR273 THR301 ASP302
Saliniquinone C	-7	TRP106 ALA107 ASN109 ASN110 CYS111 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286 LEU289
Saliniquinone D	-7.5	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Saliniquinone F	-7.5	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301

Salinosporamide B	-7.2	LYS157 LEU162 GLY163 ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Staurosporine	-7.2	TRP106 ASN109 THR265 GLY266 ASN267 CYS270 GLY271 HIS272 LYS274 ASP286
Tirandalydigin	-7.9	ASP164 VAL165 ARG166 MET208 ALA246 PRO247 PRO248 ALA249 GLN250 TYR264 THR265 GLY266 ASN267 TYR268 GLN269 TYR273 PRO299 THR301 ASP302

**Table S10:** PL<sup>pro</sup> docking results and residue interactions (category 3)

Ligands	Binding affinity (-8.0 and higher)	Interacting amino acids
Homoseongomycin	-8.5	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301
Neolymphostin A	-8.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 TYR273 THR301
Neolymphostin B	-8.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 PRO248 TYR264 ASN267 TYR268 GLN269 TYR273 THR301
Neolymphostin C	-8.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 TYR273 THR301
Neolymphostin D	-8.2	ASN109 CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273 THR301
Neolymphostinol A	-8	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 GLU161 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 PRO248 TYR264 ASN267 TYR268 GLN269 TYR273 THR301
Neolymphostinol B	-8.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO248 TYR264 ASN267 TYR268 GLN269 TYR273 THR301
Neolymphostinol C	-8	TRP106 ALA107 ASP108 ASN109 ASN110 CYS111 TYR112 LEU162 GLY163 TYR264 GLN269 CYS270 GLY271 HIS272 TYR273
Neolymphostinol D	-8.2	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 TYR273 THR301
Salinaphthoquinone D	-8.7	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 PRO248 TYR264 GLY266 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273
Saliniquinone B	-8	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 PRO247 PRO248 TYR264 TYR268 GLN269 CYS270 GLY271 TYR273 THR301

Saliniquinone E	-8	LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 MET208 SER245 ALA246 PRO247 PRO248 TYR264 ASN267 TYR268 GLN269 CYS270 GLY271 TYR273 THR301 ASP302
Salinisporamycin	-8.2	TRP106 ALA107 ASN109 ASN110 CYS111 TYR112 LYS157 LEU162 GLY163 ASP164 ARG166 GLU167 TYR264 TYR268 GLN269 CYS270 GLY271 HIS272 TYR273

**Table S11.** Predicted biological activities for candidate NPs.

<b>PASS spectra</b>	
<b>Top Ligands</b>	<b>Potential Bioactivity</b>
Bromosalinosporamide	Antiviral, Antibacterial, Anticancer, Antineoplastic, Autoimmune disease treatment, Interleukin 10 antagonist, and a Cytokine release inhibitor.
Cycloaspeptide A	Antiviral, Antifungal, Antifungal enhancer, Anticancer, Antineoplastic alkaloid, Antineoplastic enhancer, Respiratory distress syndrome treatment, , Interleukin 2 and 4 antagonist, Immunosuppressant, Toll-Like receptor antagonist, and a CC chemokine receptor 2B antagonist.
Lymphostin	Antiviral, Antineoplastic, Anticancer, Antibacterial, Antibiotic, Interleukin 1 and 1b antagonist, Immunosuppressant, and a Macrophage stimulant.
Neolymphostinol B	Antineoplastic, Anticancer, Antiviral, Thiol protease inhibitor, Leukotriene agonist, and a Macrophage colony-stimulating factor agonist.
Rifamycin B	Antiviral, Antifungal, Anti-infective, Antibiotic, Antineoplastic, Anticancer, Anti-tuberculosic, Cytochrome P450 stimulant, Immunostimulant, Histidine kinase inhibitor, Beta glucuronidase inhibitor, Cytokine release inhibitor, and a T cell inhibitor.
Salinaphthoquinone B	Antiviral, Antiseptic, Antineoplastic, Anti-parasitic, Antibacterial, Anti-infective, Antifungal, Anti-inflammatory, Anti-tuberculosic, Antioxidant, Free radical scavenger, Hepatoprotectant, Immunosuppressant, Kinase inhibitor, Histidine kinase inhibitor, and a Histamine release inhibitor.
Salinaphthoquinone E	Antineoplastic, Anticancer, Antifungal, Antifungal enhancer, Anti-inflammatory, Immunosuppressant, Interleukin 1, 2, 5, 10 antagonist, Antibacterial, Anti-parasitic, Antibiotic, Beta glucuronidase inhibitor, Kinase inhibitor, Histidine kinase inhibitor, Antioxidant, T cell inhibitor, Cytokine release inhibitor, Histamine release inhibitor, and an Expectorant.

Salinipostin A	Antiviral, Anti-diabetic, Anticancer, Toll-Like receptor antagonist, Histamine release stimulant, Alpha-glucuronidase inhibitor, Lipase inhibitor, Rhizopuspepsin inhibitor, Transcription factor NF kappa B stimulant, and a Macrophage colony-stimulating factor agonist.
Salinipostin C	Antiviral, Anti-diabetic, Anticancer, Lipase inhibitor, Alpha-glucuronidase inhibitor, Rhizopuspepsin inhibitor, Toll-Like receptor antagonist, Histamine release stimulant, Leukotriene agonist, Transcription factor NF kappa B stimulant, and a Macrophage colony-stimulating factor agonist.
Saliniquinone F	Antifungal, Antibacterial, Anti-parasitic, Anticancer, Antineoplastic, Antioxidant, Kinase inhibitor, Histidine kinase inhibitor, Antiseptic, Histamine release inhibitor, Free radical scavenger, Transcription factor NF kappa B stimulant, Respiratory analeptic, Beta glucuronidase inhibitor, and a Leukotriene synthesis inhibitor.
Salinosporamide C	Antiviral, Anticancer, Antineoplastic, Respiratory analeptic, protease inhibitor, Transcription factor NF kappa B stimulant, JAK2 expression inhibitor, Histidine kinase inhibitor, Interleukin 10 antagonist.
Salinosporamide I	Antiviral, Antifungal, Anti-asthmatic, Antineoplastic alkaloid, Antibacterial, Anticancer, protease inhibitor, Autoimmune disorders treatment, Cytokine release inhibitor, and an Interleukin 10 antagonist.
Salinilactam	Antiviral, Anti-infective, Antibacterial, Anti-tuberculosic, Antioxidant, Antineoplastic alkaloid, Anticancer, Antibiotic, Anti-parasitic, Antifungal, Antifungal enhancer, Beta glucuronidase inhibitor, Immunosuppressant, Transcription factor NF kappa B stimulant, Interferon-gamma antagonist, Cytokine release inhibitor, and Interleukin 10 antagonist
Sporolide A	An antineoplastic alkaloid, Antioxidant, Anticancer, Antibiotic, Beta glucuronidase inhibitor, Antifungal, Antibacterial, Immunosuppressant, Interleukin 1 and 10 antagonist, Histidine kinase inhibitor, Cytokine release inhibitor, and a Transcription factor NF kappa B stimulant.