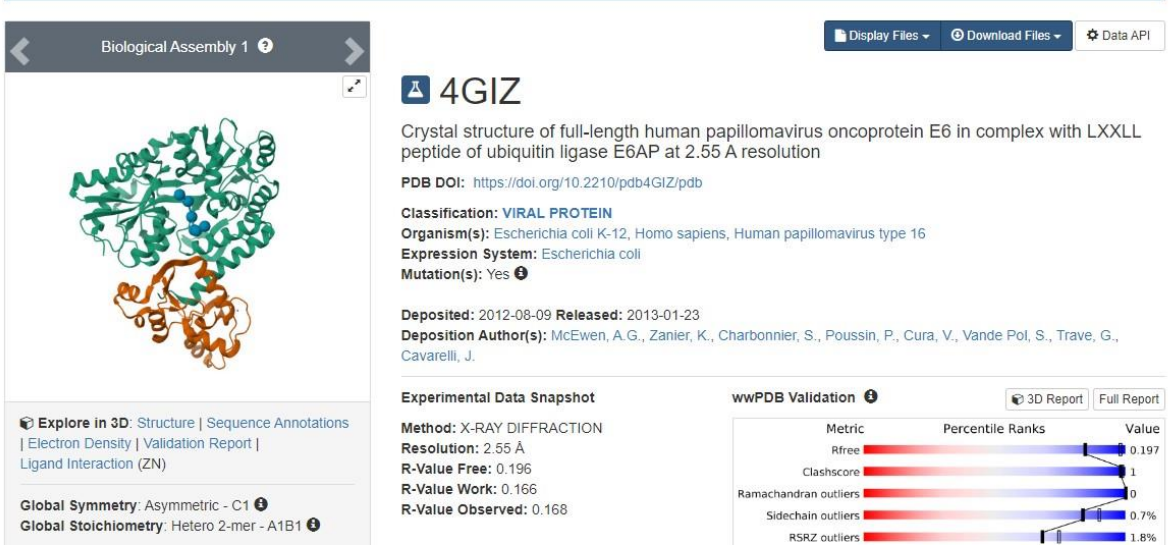
CADD PROJECT

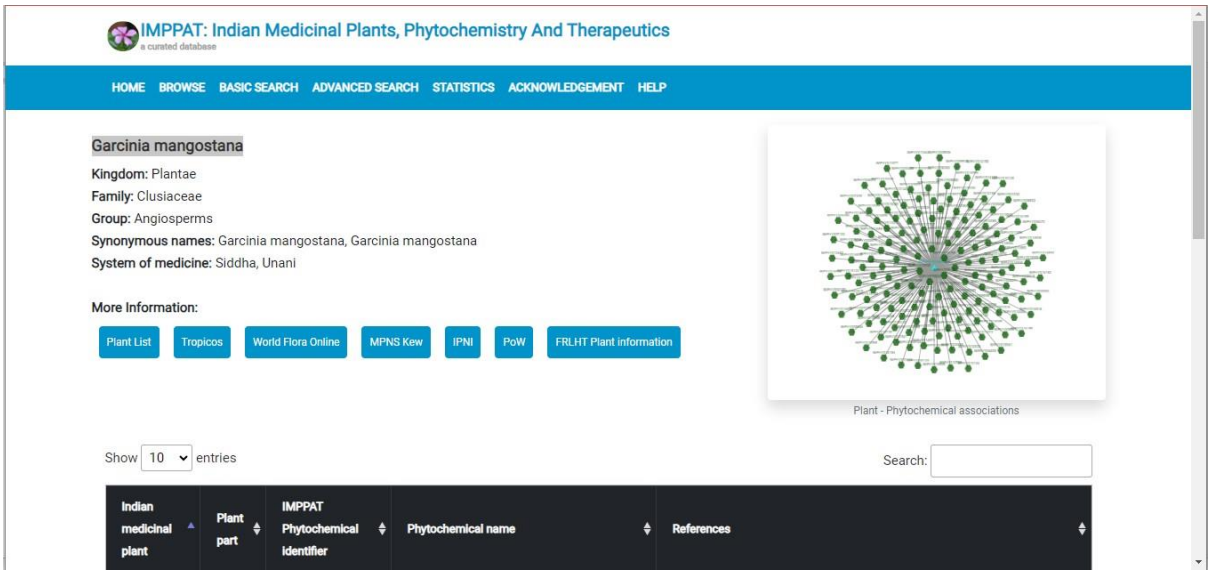
CERVICAL CANCER

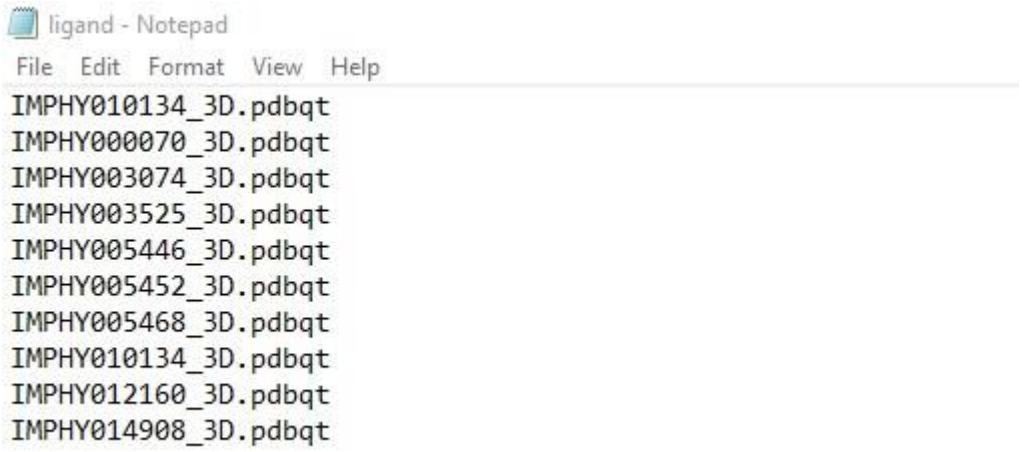
Cervical cancer (CC) is the fourth most common disease in women worldwide, and it significantly affects poor nations due to insufficient funding, limited access to healthcare, and monitoring challenges. The primary cause of CC is the human papillomavirus (HPV), and although preventive vaccinations have been approved, patients with pre-existing infections or HPV-induced carcinomas are not adequately treated. The high-risk (HR) HPV E6 and E7 oncoproteins are biomarkers for the progression of cervical cancer. The E6 structure has been extensively studied since its resolution, with the aim of developing new and effective treatments for cervical cancer. To this end, several small molecules, both plant-derived and synthetic, have been identified as inhibitors of the E6 oncoprotein. Computational-aided methods have played a crucial role in the discovery and development of these molecules, reducing the time and cost of drug development. This review will discuss the small molecules that are currently being explored as blockers of the HR HPV E6 protein, as well as the in silico approaches used to design new therapeutics for managing cervical cancer. Additionally, the review will briefly touch on future perspectives in cervical cancer therapy.

Protein: 4GIZ



Ligand: IMPPAT Database: Garcinia mangostana





AutoDock Vina:

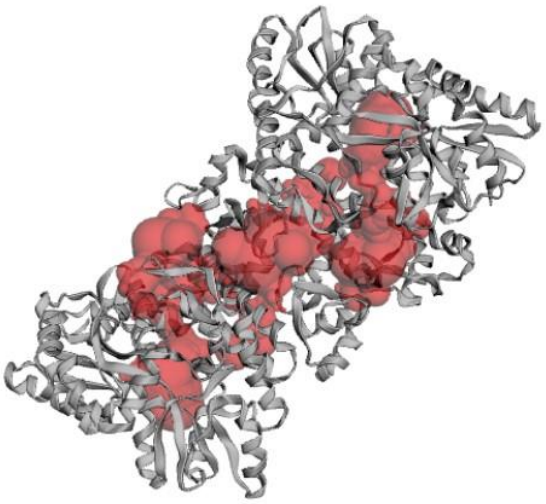
Active Site : CASTp

4GIZ

Crystal structure of full-length human papillomavirus oncoprotein E6 in complex with LXXLL peptide of ubiquitin ligase E6AP at 2.55 A resolution

Other assembly help

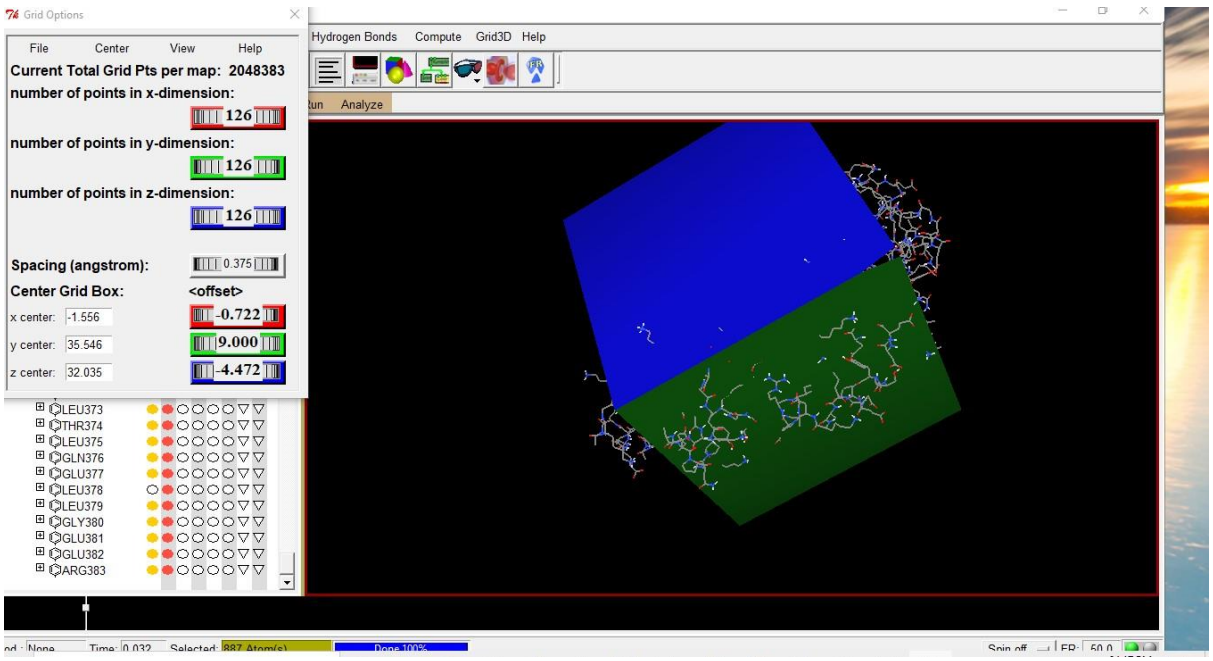
4GIZ1



PocID help	Area (SA) Å^2	Volume (SA) Å^3
1	4991.068	5069.467

PocID	Chain	SeqID	AA	Atom
1	A	383	ARG	NH1
1	A	383	ARG	NH2

Grid preparation:



Config File:

config - Notepad

File Edit Format View Help

```
receptor = 4giz.pdbqt


center_x=-1.556
center_y=35.546
center_z=32.035


size_x = 126
size_y = 126
size_z = 126

num_modes = 10
energy_range = 4
```

Vina Script:

C:\Users\DELL\Documents\docking\vina.pl - Notepad++

File Edit Search View Encoding Language Settings Tools Macro Run Plugins Window ?

vina.pl | template.fasta | align.py | rcsb_pdb_7EU8.fasta

```
#!/usr/bin/perl
print"Ligand_file:\t";
$ligfile=<STDIN>;
chomp $ligfile;
open (FH,$ligfile)||die
"Cannot open file\n";
@arr_file=<FH>;
for($i=0;$i<@arr_file;$i++)
{
   print"@arr_file[$i]\n";
   @name=split(/\./,@arr_file[$i]);
}
for($i=0;$i<@arr_file;$i++)
{
   chomp @arr_file[$i];
   print"@arr_file[$i]\n";
   system("vina.exe --config config.txt --ligand @arr_file[$i] --log @arr_file[$i]_log.log");
}
```

Result:

```
IMPHY010134_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY010134_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1471330328
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.0      0.000      0.000
   2         -7.9      5.282      8.291
   3         -7.6      2.505      4.987
   4         -7.3      1.714      2.573
   5         -7.3      4.635      7.388
   6         -7.1     20.712     25.813
   7         -7.1      2.303      8.881
   8         -7.0     20.423     22.737
   9         -7.0     19.315     22.287
  10         -6.8     19.804     22.940
Writing output ... done.
```

```
IMPHY000070_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY000070_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1221661720
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.9      0.000      0.000
   2         -7.4     16.043     18.486
   3         -7.0      1.106      3.797
   4         -6.7      1.607      4.887
   5         -6.6      0.965      4.813
   6         -6.2     17.853     20.487
   7         -6.2      5.067      7.313
   8         -5.9      5.738      8.932
   9         -5.9     16.334     18.110
  10         -5.8     15.568     17.367
Writing output ... done.
```

```
IMPHY003074_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY003074_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1285897424
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.3      0.000      0.000
   2         -8.1      1.879      2.522
   3         -7.6      4.577      7.561
   4         -7.2     10.732     13.160
   5         -7.2     18.532     22.262
   6         -7.1     19.001     22.507
   7         -6.9     16.521     19.655
   8         -6.6      4.531      7.914
   9         -6.5     16.935     20.201
  10         -6.5     15.929     18.916
Writing output ... done.
```

```
IMPHY003525_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY003525_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1811700928
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -4.4      0.000      0.000
   2         -4.3      2.533      4.916
   3         -4.1      1.820      3.136
   4         -4.0     17.111     18.708
   5         -3.9     16.219     18.070
   6         -3.9      2.404      2.725
   7         -3.7      3.506      4.315
   8         -3.7     17.560     20.091
   9         -3.6     15.704     17.052
  10         -3.5      3.040      4.465
Writing output ... done.
```

```
IMPHY005446_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY005446_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 71836312
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.3      0.000      0.000
   2         -8.0      3.245      7.622
   3         -7.9      3.625      6.264
   4         -7.8     20.568     22.154
   5         -7.6      2.119      2.662
   6         -7.6      2.971      7.352
   7         -7.5     20.472     23.311
   8         -7.4     20.505     22.281
   9         -7.4      1.802      2.631
  10         -7.4      1.699      6.914
```

```
IMPHY005452_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY005452_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1652485620
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.6      0.000      0.000
   2         -8.5      2.110      3.215
   3         -8.3     20.593     24.429
   4         -8.3     19.260     24.203
   5         -8.2     18.401     20.677
   6         -8.1     19.205     23.152
   7         -8.0     20.393     24.481
   8         -8.0     19.039     20.932
   9         -7.9     20.588     23.432
  10         -7.6     19.265     22.236
Writing output ... done.
```

```
IMPHY005468_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY005468_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -956844912
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.4      0.000      0.000
   2         -7.4     18.221     19.479
   3         -7.3      0.899      5.751
   4         -7.2     18.018     19.035
   5         -7.0     18.352     19.288
   6         -6.7     22.532     24.860
   7         -6.6     22.651     25.041
   8         -6.5      1.624      6.381
   9         -6.4     12.499     14.750
  10         -6.1     11.508     12.855
Writing output ... done.
```

```
IMPHY010134_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY010134_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1087137000
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.9      0.000      0.000
   2         -7.4     17.880     20.549
   3         -7.3     17.477     18.814
   4         -7.1     16.858     20.648
   5         -6.8     16.474     21.432
   6         -6.8     18.165     20.785
   7         -6.8      4.508      7.789
   8         -6.7      4.228      7.211
   9         -6.6     18.211     20.479
  10         -6.6     12.759     17.595
Writing output ... done.
```

```
IMPHY012160_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY012160_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1452484096
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -5.7      0.000      0.000
   2         -5.7      2.871      4.896
   3         -5.5     18.077     18.802
   4         -5.5      1.868      4.286
   5         -5.3      1.594      2.488
   6         -5.2      3.813      5.898
   7         -5.1      2.374      5.296
   8         -4.9     19.413     19.765
   9         -4.8     17.139     18.656
  10         -4.7      2.312      4.368
Writing output ... done.
```

```
IMPHY014908_3D.pdbqt
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
# DOI 10.1002/jcc.21334                                         #
#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Output will be IMPHY014908_3D_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 123490816
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -8.0      0.000      0.000
   2         -7.7      1.416      6.985
   3         -7.7      0.729      1.486
   4         -7.5     18.429     19.787
   5         -7.5      7.537     11.048
   6         -7.3      2.154      7.219
   7         -7.2     18.189     20.267
   8         -7.2      2.072      6.836
   9         -7.1     23.329     24.921
  10         -7.0     13.781     16.047
```