Supplementary Materials

Assessing Molecular Docking Tools to Guide Targeted Drug Discovery of CD38 Inhibitors

Eric D. Boittier 1, Yat Yin Tang 1,2, McKenna E. Buckley 2, Zachariah P. Schuurs 1,3, Derek J. Richard 1 and Neha S. Gandhi 1,3,*

1 Cancer & Ageing Research Program, Institute of Health and Biomedical Innovation at the Translational Research Institute (TRI), Queensland University of Technology (QUT), Brisbane, Queensland 4102, Australia; boittier@qut.edu.au (E.D.B.); yatyin.tang@connect.qut.edu.au (Y.Y.T.);
zachariah.schuurs@hdr.qut.edu.au (Z.P.S.); derek.richard@qut.edu.au (D.J.R.)
2 School of Chemistry and Physics, Faculty of Science and Engineering, Queensland University of Technology, Brisbane, QLD 4000, Australia; mckenna.buckley@connect.qut.edu.au
3 School of Mathematical Sciences, Faculty of Science and Engineering, Queensland University of Technology, Brisbane, QLD 4000, Australia

* Correspondence: neha.gandhi@qut.edu.au; Tel.: +(61)-7-3138-7394

Received: 28 May 2020; Accepted: 14 July 2020; Published: date
Figure S1. Superposition of a series of ligands in the active site: (a) beta-nicotinamide ribose monophosphate ligands (tan: 3DZK, blue: 3DZJ, pink: 4OGW, green: 2HCT), (b) di- and triphosphoriboses (tan: 4TMF, blue: 2I67, pink: 3DZH) and (c) NAD and derivatives (tan: 2O3U, blue: 6EDR, pink: 4F45, green: 2I65). Water is shown as red spheres.
Figure S2. Correlation between number of active rotatable bonds and RMSD for the programs like (a) AutoDock 4, (b) Vina, (c) Glide, (d) Gold, (e) PLANTS, (f) Molegro and (g) rDock assessed in this study. Spearman’s rank correlation and associated $p$ values at the 95% confidence interval are reported (here, the null hypothesis is that there is a correlation). Based on these limited results, AutoDock4, Gold, Molegro and rDock appeared to be particularly affected with ligands with high conformational degrees of freedom.
Table S1. Structures of ligands used to assess scoring power.

| Chemical Formula | Structure | IC50 nM | S.D | Number |
|------------------|-----------|---------|-----|--------|
| C_{8}H_{16}F_{4}N_{3}O | ![Structure 1](attachment:structure1.png) | 510 | 100 | 1a |
| C_{8}H_{19}F_{4}N_{6}O | ![Structure 2](attachment:structure2.png) | 72 | 13 | 1b |
| C_{8}H_{17}F_{4}N_{7}O | ![Structure 3](attachment:structure3.png) | 450 | 81 | 1c |
| C_{8}H_{16}F_{4}N_{6}O | ![Structure 4](attachment:structure4.png) | 2300 | 37 | 1d |
$C_{20}H_{16}F_4N_8O$ 4300 210 1e

$C_{19}H_{17}F_4N_7O$ 1600 610 1f

$C_{19}H_{17}F_4N_7O$ 6800 4800 1g

$C_{19}H_{17}F_4N_7O$ 8000 2400 1h
\[
\text{C}_{31}\text{H}_{16}\text{F}_{4}\text{N}_{6}\text{O}_{2}
\]

4200 200 1i

\[
\text{C}_{31}\text{H}_{16}\text{F}_{4}\text{N}_{6}\text{O}_{2}
\]

3400 1800 1j

\[
\text{C}_{31}\text{H}_{16}\text{F}_{4}\text{N}_{6}\text{O}_{2}
\]

5500 1600 1k

\[
\text{C}_{22}\text{H}_{19}\text{F}_{4}\text{N}_{7}\text{O}
\]

1900 120 1l

\[
\text{H}_2\text{N}\text{C}=\text{O}
\]

\[
\text{H}_2\text{N}\text{C}=\text{O}
\]

\[
\text{H}_2\text{N}\text{C}=\text{O}
\]

\[
\text{H}_2\text{N}\text{C}=\text{O}
\]
Figure S3. rDock scoring performance.

Figure S4. Analysis of additive, “ligand” bias (bias towards better scoring as number of heavy atoms increases) observed in the top performing programs in the scoring power tests. Ligand efficiency (in this context, the score divided by number of heavy atoms) can be used as a measure of “ligand” bias. For a docking score that correlates with ligand efficiency, it is assumed that there is no ligand bias. Pearson’s correlation and associated $p$ values at the 95% confidence interval are reported (here, the null hypothesis is that there is a correlation between ligand efficiency and docking score) for (a) Glide, (b) Vina, (c) Plants and (d) Gold scores. Plants and Gold showed no correlation between ligand efficiency and docking score, which suggests that the scoring functions may be subject to ligand bias. Glide showed a strong correlation. Vina showed a small, but statistically significant, correlation between ligand efficiency.