

## Supplementary Materials

# Field-based Affinity Optimization of a Novel Azabicyclohexane Scaffold HIV-1 Entry Inhibitor

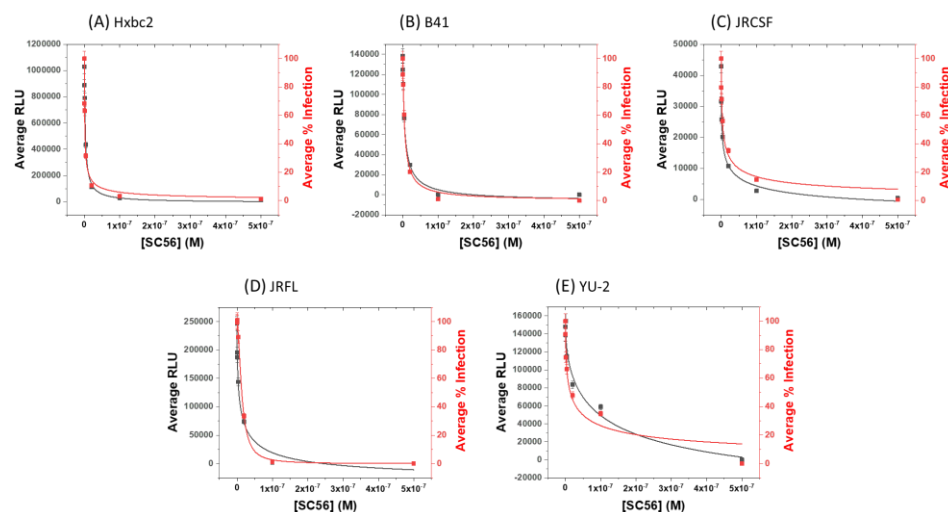
Megan E. Meuser<sup>1</sup>, Adel A. Rashad<sup>1</sup>, Gabriel Ozorowski<sup>2</sup>, Alexej Dick<sup>1</sup>, Andrew B. Ward<sup>2</sup> and Simon Cocklin<sup>1,\*</sup>

<sup>1</sup> Department of Biochemistry & Molecular Biology, Drexel University College of Medicine, Rooms 10307, 10309, and 10315, 245 North 15th Street, Philadelphia, PA 1910, USA; mem484@drexel.edu (M.E.M.); aaa396@drexel.edu (A.A.R.); ad3474@drexel.edu (A.D.)

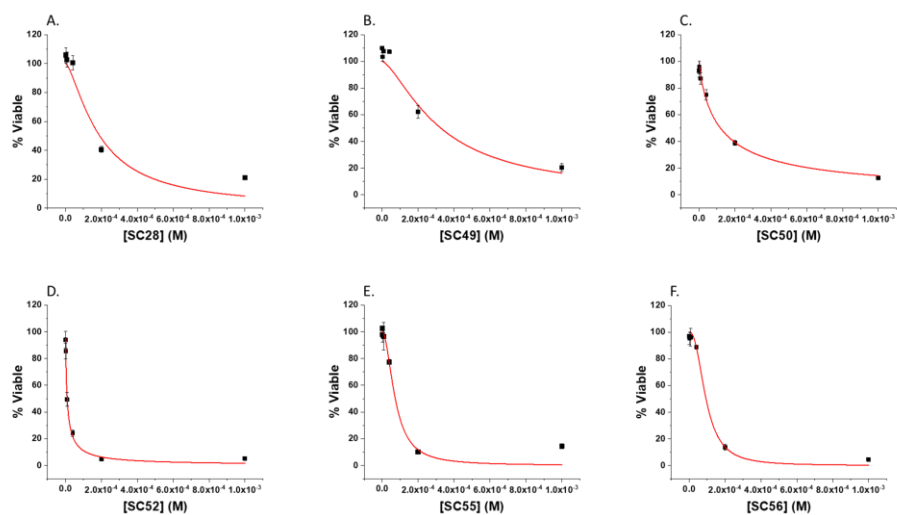
<sup>2</sup> Department of Integrative Structural and Computational Biology, Collaboration for AIDS Vaccine Discovery, The Scripps Research Institute, La Jolla, CA 92037, USA; gozorows@scripps.edu (G.O.); andrew@scripps.edu (A.B.W.)

\* Correspondence: sc349@drexel.edu; Tel.: 215-762-7234 (Office); 215-762-4979 (Lab); Fax: 215-762-4452

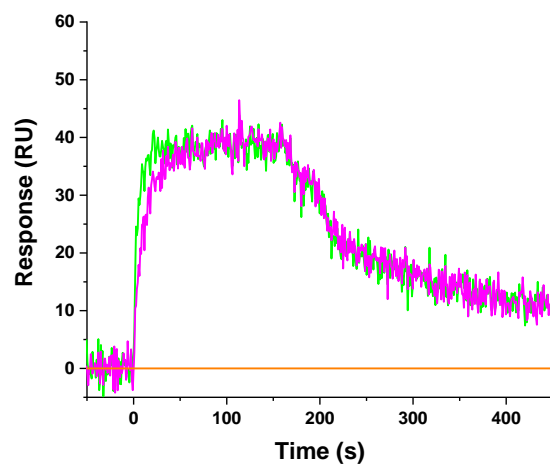
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**Figure S1.** Single round infection assay graphs, using SC56 (starting concentration 5 $\mu$ M with 1:5 serial dilutions) as an example, against pseudoviruses with envelopes derived from (A) HxBc2 (B) B41 (C) JRCSF (D) JRFL and (E) YU-2. The left axis (black) represents the average relative luciferase units while the right axis (red) represents the average % infection. A non-linear regression logistic fit of data points from which the IC<sub>50</sub> values were derived is shown. Error bars indicate the standard deviation from at least three individual replicates.



**Figure S2.** Toxicity of compounds (A) SC28, (B) SC49, (C) SC50, (D) SC52, (E) SC55, and (F) SC56 starting at 1mM with 1:10 dilutions using U87 cells. Red line represents the logistic fit of the data points from which the  $CC_{50}$  was derived. Error bars indicate the standard deviation from three individual replicates.



**Figure S3.** Sensorgrams depicting 12.5  $\mu$ M (green) and 6.25  $\mu$ M (magenta) SC56 over a surface to which 13000 RUs of B41 SOSIP.664 gp140 trimer had been immobilized. The theoretical  $R_{max}$  for this surface is 41 RUs. As can be seen, both concentrations saturate the surface.