

Tutorial Virtual-Screening Workflows and Prospective Results from the Teach-Discover-Treat Competition 2014 against Malaria

SUPPLEMENTARY MATERIAL

Sereina Riniker,^{1*} Gregory Landrum,² Floriane Montanari,³ Santiago D. Villalba,⁴ Julie Maier,⁵ Johanna M. Jansen,⁶ W. Patrick Walters,⁷ Anang A. Shelat^{5*}

¹ *Laboratory of Physical Chemistry, ETH Zürich, Vladimir-Prelog-Weg 2, 8093 Zürich, Switzerland*

² *T5 Informatics GmbH, Spalenring 11, 4055 Basel, Switzerland*

³ *University of Vienna, Department of Pharmaceutical Chemistry, Pharmacoinformatics Research Group, Althanstrasse 14, 1090 Vienna, Austria*

⁴ *IMP - Research Institute of Molecular Pathology, Campus-Vienna-Biocenter 1, 1030 Vienna, Austria*

⁵ *Department of Chemical Biology & Therapeutics, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105, USA*

⁶ *Department of Global Discovery Chemistry, Novartis Institutes for BioMedical Research, 5300 Chiron Way, Emeryville, CA 94608, USA*

⁷ *Relay Therapeutics, 215 First Street, Cambridge, MA 02142*

Email: sriniker@ethz.ch

Email: anang.shelat@stjude.org

Table S1. Results from the follow-up assay for the 31 compounds that were in the primary HTS screen: EC50 values, the final scores (active or inactive), and the ranks in the workflows 1 and 2. Partially active or single-point active compounds were considered inactives (marked by italic font). ChEMBL-NTD datasets: (N) Novartis-GNF Malaria Box (N) [1], St. Jude Children's Research Hospital Dataset (J) [2], GSK TCAMS (G) [3], DNDi HAT set (D). Compounds marked with (P) were tested in PubChem assays.

Identifier	EC50 [µM]	Score	Rank (1000) Workflow 1	Rank (top 10'000) Workflow 1	Rank (top 1000) Workflow 2	HTS screen	Known Datasets
SJ000027935	0.29	Active		646	618	Active	N, J (active)
SJ000027937	0.35	Active		1812	678	Ambiguous	N, J, P (active)
SJ000171111	0.36	Active		508	126	Active	N, J (active)
SJ000082805	0.37	Active		-	727	Active	N, J, G, P (active)
SJ000243624	0.41	Active		395	349	Active	N, J (active)
SJ000127662	0.43	Active		3407	490	Active	J (active)
SJ000154494	0.44	Active	44	106		Active	J (inactive)
SJ000140382	0.45	Active		-	443	Active	J (active)
SJ000147013	0.49	Active		4682	239	Active	
SJ000171307	0.52	Active		431	310	Active	N, J (active)
SJ000147025	0.57	Active		4431	232	Active	
SJ000180705	0.59	Active	425	2764	589	Active	J (active)
SJ000197041	0.62	Active		-	997	Active	

SJ000170251	0.85	Active		-	460	Ambi- guous	N, J, P (active)
SJ000243360	1.2	Active		-	609	Ambi- guous	
SJ000281068	1.3	Active		-	733	Active	J (active)
SJ000243361	1.9	Active		5868	450	Ambi- guous	J (active)
SJ000243592	2.0	Active	144	572	542	Active	J (active)
SJ000011369	2.3	Active		2833	534	Active	J (active)
SJ000291576	2.3	Active		8329	862	Active	
SJ000143975	2.3	Active		8797	892	Active	J, P (active)
SJ000147376	2.4	Active		4440	489	Active	J, P (active)
SJ000192808	2.6	Active		5442	958	Active	N, J (active)
SJ000144869	3.0	Active		4679	946	Active	J (active)
SJ000146674	3.1	Active		844	466	Active	
SJ000140380	3.3	Active		-	498	Ambi- guous	J (active)
SJ000113373	3.7	Active		2399	670	Active	J, D (active)
SJ000127976	3.8	Active		5479	926	Active	
SJ000137729	9.0	Active	128	474	913	Active	J (active)
SJ000143737	15.0	Active	887	6694		Ambi- guous	
SJ000298473		Inactive	837	6285		Inactive	

References

- [1] F.-J. Gambo, L. M. Sanz, J. Vidal, C. de Cozar, E. Alvarez, J.-L. Lavandera, D. E. Vanderwall, D. V. S. Green, V. Kumar, S. Hasan, J. R. Brown, C. E. Peishoff, L. R. Cardon, J. F. Garcia-Bustos, Thousands of chemical starting points for anti-malarial lead identification. *Nature*, 465, 305-310 (2010).
- [2] W. A. Guiguemde, A. A. Shelat, D. Bouck, S. Duffy, G. J. Crowther, P. H. Davis, D. C. Smithson, M. Connelly, J. Clark, F. Zhu, M. B. Jimenez-Diaz, M. S. Martinez, E. B. Wilson, A. K. Tripathi, J. Gut, E. R. Sharlow, I. Bathurst, F. El Mazouni, J. W. Fowble, I. Forquer, P. L. McGinley, S. Castro, I. Angulo-Barturen, S. Ferrer, P. J. Rosenthal, J. L. DeRisi, J. S. Lazo, D. S. Roos, M. K. Riscoe, M. A. Phillips, P. K. Rathod, W. C. Van Voorhis, V. M. Avery, R. K. Guy, Chemical genetics of *Plasmodium falciparum*, *Nature*, 465, 311-315 (2010).
- [3] Novartis-GNF Malaria Box, K. Gagaring, R. Borboa, C. Francek, Z. Chen, J. Buenviaje, D. Plouffe, E. Winzeler, A. Brinker, T. Diagana, J. Taylor, R. Glynne, A. Chatterjee, K. Kuhen. Genomics Institute of the Novartis Research Foundation (GNF), 10675 John Jay Hopkins Drive, San Diego CA 92121, USA and Novartis Institute for Tropical Disease, 10 Biopolis Road, Chromos # 05-01, 138 670 Singapore.