

Divergent Modulation of Src-Family Kinase
Regulatory Interactions with ATP-Competitive
Inhibitors

Supporting Information

Stephen E. Leonard, Amy C. Register, Ratika Krishnamurty, Gabriel J. Brighty, and
Dustin J. Maly

Affiliations: Department of Chemistry, University of Washington, Seattle, WA 98195, USA

Contact: maly@chem.washington.edu

Src SH3 Pulldown

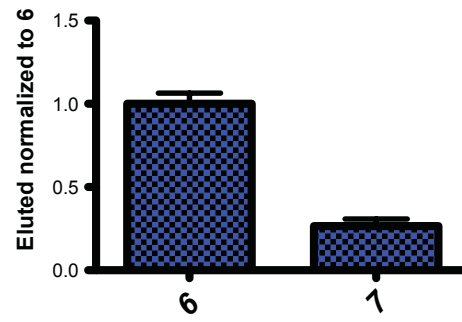


Figure S1. Quantification of the pull-down experiments performed with Src^{S245C} in the presence of **6** or **7**. (mean +/- SEM, n=3).

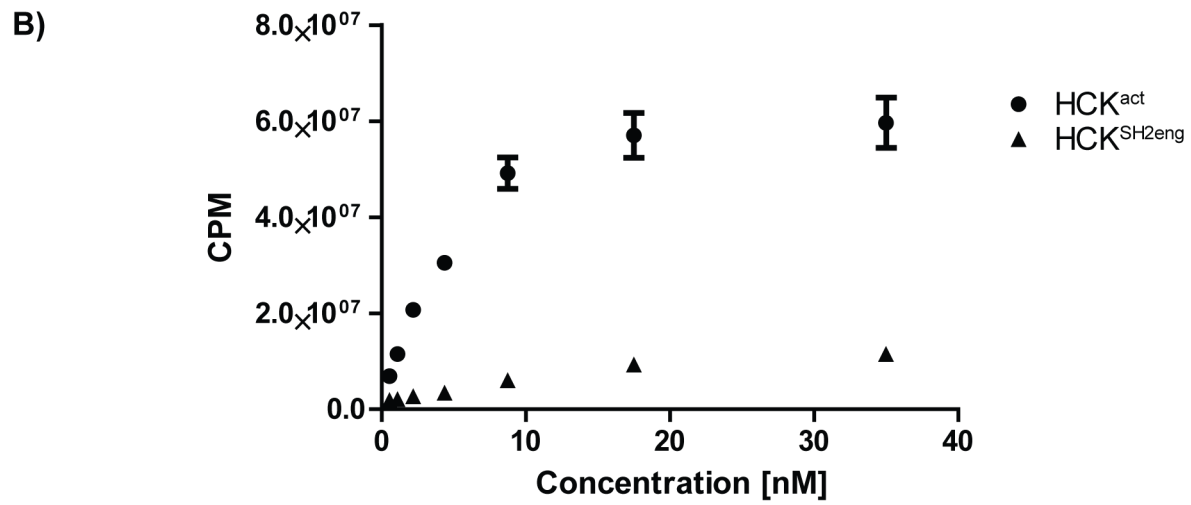
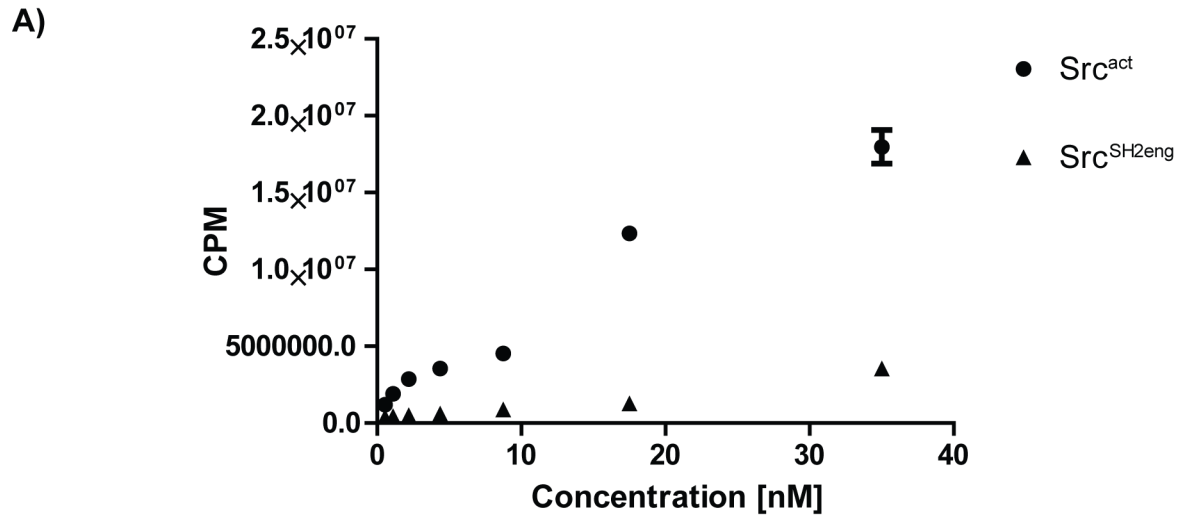


Figure S2. Catalytic activity of SFK constructs. A) Activity assay with Src^{act}, Src^{Y527F} or Src^{SH2eng}. B) Activity assay with Hck^{act}, Hck^{Y527F} or Hck^{SH2eng}.

Table S1. K_i values (nM) for drug resistant constructs.

	Csk^{DR}	Src^{Y527F}	Hck^{Y527F}
1	>10000	80	164
2	1420	23	6.6
3	848	5200	1336
4	nt	<6	<6
5	498	<6	<6

Table S2. pY527 chemical genetic assay parameters.

Inhibitor	1	2	5
%Src bound	92	85	97
%Hck bound	86	98	97
%Csk^{DR} bound	9	9	10
[Inhibitor] nM	1000	150	55

Table S3. K_i values (nM) for covalent inhibitors.

	Src^{Y527F}	Src^{S245C}	Hck^{Y527F}	Hck^{S245C}
6	350	<6	648.1	<6
7	>10000	<6	603	<6

Table S4. Activity of SFK treated with covalent inhibitors for pY527 Assay.

Inhibitor	Untreated	6	7
Src % Activity	100	0	0
Hck % Activity	100	0	0

Table S5. K_i values (nM) for SFKs.

	Src ^{SH2eng}	Src ^{Act}	Hck ^{SH2eng}	Hck ^{Act}
1	81	43	67	31
2	<20	110	17	83
3	44	1400	<10	83
4	<20	<0.5	<10	<0.5
5	<20	<0.5	<10	<0.5
8	187	1200	60	1100
9	1280	66	86	12
10	164	33	85	7
11	420	18	329	14
12	250	39	33	0.7