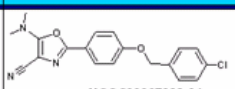
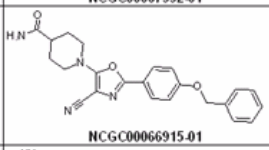
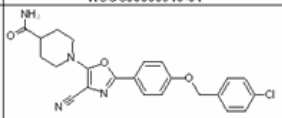
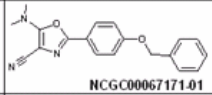
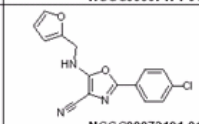
Probe Report
NIH Chemical Genomics Center
Pyruvate Kinase (*bacillus stearothermophilus*)

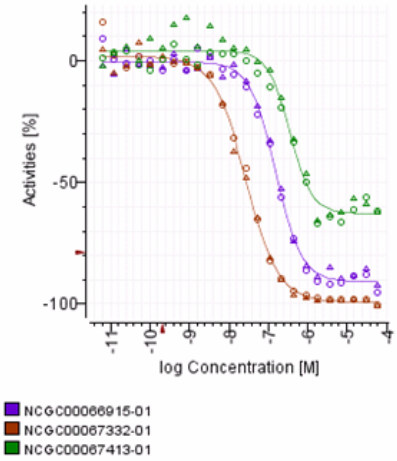
Target and assay description:
Pyruvate kinase (partially purified from Bacillus stearothermophilus) was assayed for its ability to generate ATP from ADP using phosphoenolpyruvate (PEP) as a substrate. ATP generation was detected in a coupled reaction by luciferase-mediated luminescence, an ATP-dependent process. Pyruvate kinase substrates, PEP and ADP, were present in the assay at Km and 10-fold below Km respectively. The enzyme was assayed at an intermediate level of activity to screen for inhibitors and activators. In addition, ribose 5 phosphate, a positive modulator of pyruvate kinase, was included in the assay at AC10 in order to identify possible potentiators.

PubChem Assay ID: 361, http://pubchem.ncbi.nlm.nih.gov/assay/assay.cgi?aid=361
Date of Report: November 21, 2006

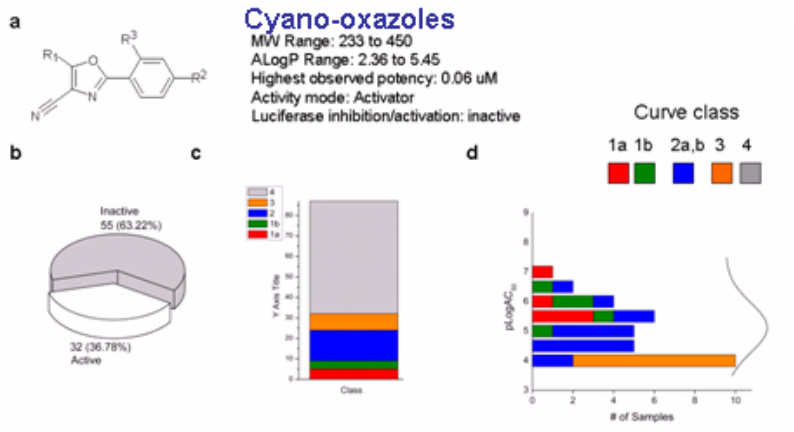
***Inhibitors* of Pyruvate Kinase**

#	Pubchem ID	NCGC ID	AC50 (uM)	% Purity	MW	ALog P	Supplier	Supplier ID
1	862236	 NCGC00067332-01	0.03	99.7	354	4.51	InterBioScreen	MLS000042013
2	862906	 NCGC00066915-01	0.16	99.8	403	3.49	InterBioScreen	MLS000041866
3	862867	 NCGC00067413-01	0.36	99.8	437	4.15	InterBioScreen	MLS000042015
4	863314	 NCGC00067171-01	2.8	*	319	3.86	InterBioScreen	MLS000041864
5	4257445	 NCGC00072191-01	inactive	*	300	4.07	Chembridge	MLS000061467

Curves from re-supplied compound

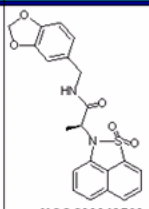
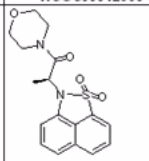
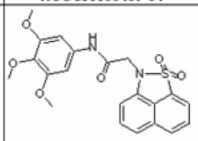
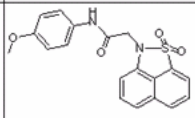
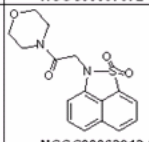


The * in %Purity represents compounds where only primary qHTS data was obtained.

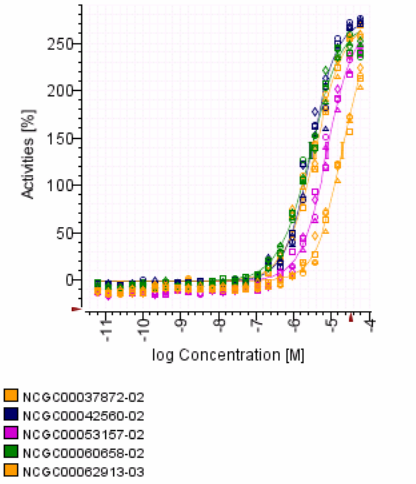


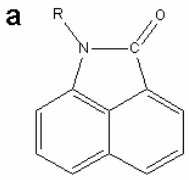
Probe SAR summary. **a)**. Core structure, associated potency and physicochemical properties. **b)**. Number of active and inactive analogs. **c)**. Distribution of analog activity with respect to qHTS curve classes. **d)**. Potency distribution for active analogs.

Activators of Pyruvate Kinase

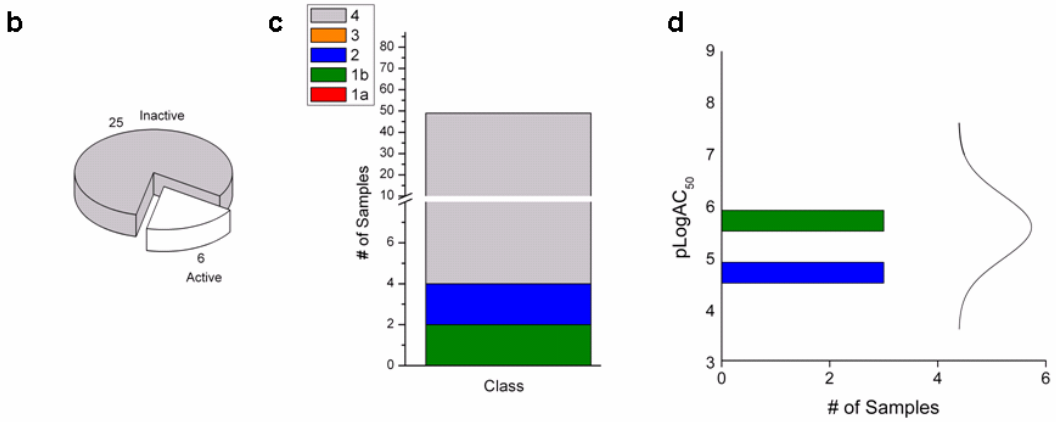
#	Pubchem ID	NCGC ID	AC50 (uM)	% Purity	MW	ALog P	Supplier	Supplier ID
1	3712493	 NCGC00042560-01	0.60	92.9	410	2.78	Enamine	MLS000053480
2	4257018	 NCGC00053157-01	1.8	98.1	346	1.6	ChemBridge	MLS000065018
3	4264712	 NCGC00060658-01	2.2	97.2	429	3.01	ChemBridge	MLS000254524
4	3711650	 NCGC00037872-01	4.0	100	368	3	Enamine	MLS000081977
5	4265644	 NCGC00062913-01	16	99	332	1.21	ChemBridge	MLS000064714

Curves from re-supplied compound





Napthalene lactam
MW Range: 197 to 463
ALogP Range: 1.9 to 5.1
Activity mode: Activator
Luciferase inhibition/activation: inactive



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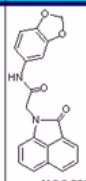
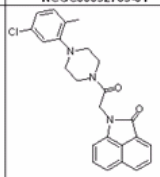
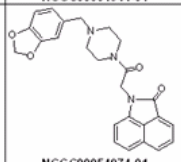
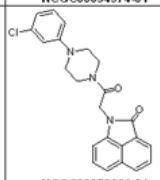
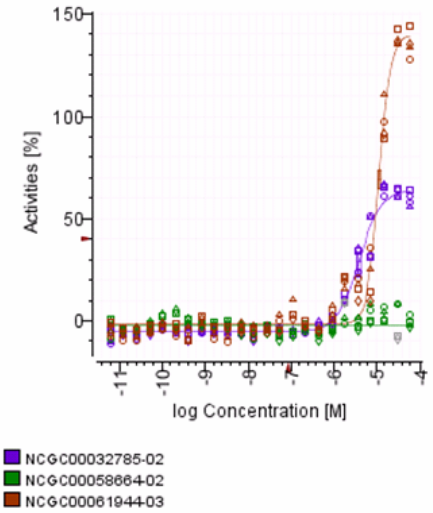
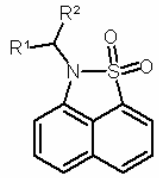
#	Pubchem ID	NCGC ID	AC50 (uM)	% Purity	MW	ALogP	Supplier	Supplier ID
1	848645	 NCGC00032785-01	0.35	97.8	346	3.17	Asinex Ltd.	MLS000035877
2	4262855	 NCGC00061944-01	6.3	98.8	420	4.11	ChemBridge	MLS000049241
3	4259672	 NCGC00054974-01	216	*	430	2.87	ChemBridge	MLS000096964
4	4265745	 NCGC00058664-01	inactive	99.6	406	3.8	ChemBridge	MLS000096904

The * in %Purity represents compounds where only primary qHTS data was obtained.

Curves from re-supplied compound

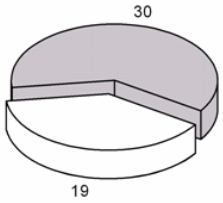


a

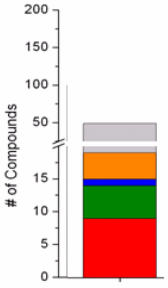


Napthalene sulfams
MW Range: 247 to 448
ALogP Range: 1.2 to 4.4
Highest observed potency: 0.8 uM
Activity mode: Activator
Luciferase inhibition/activation: inactive

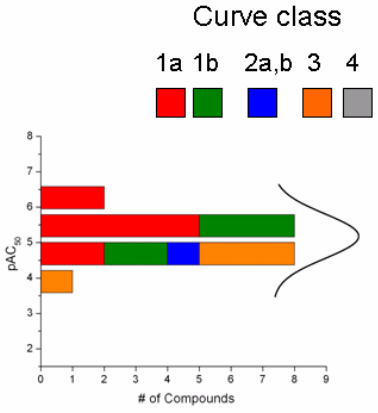
b



c



d



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