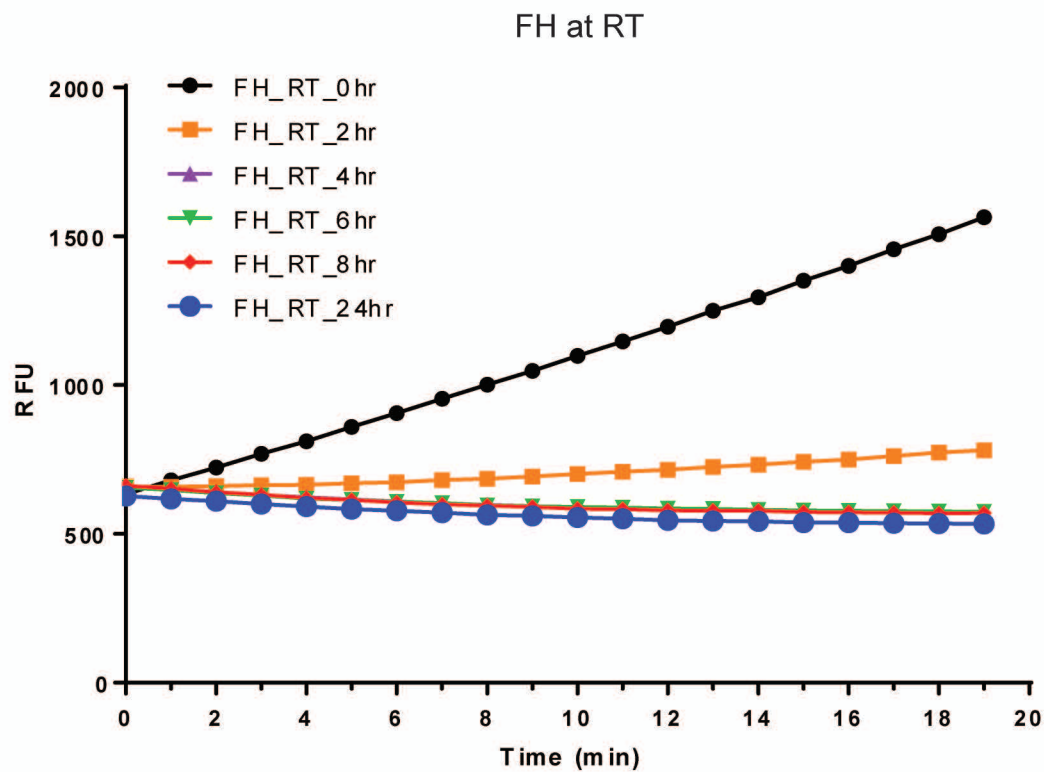
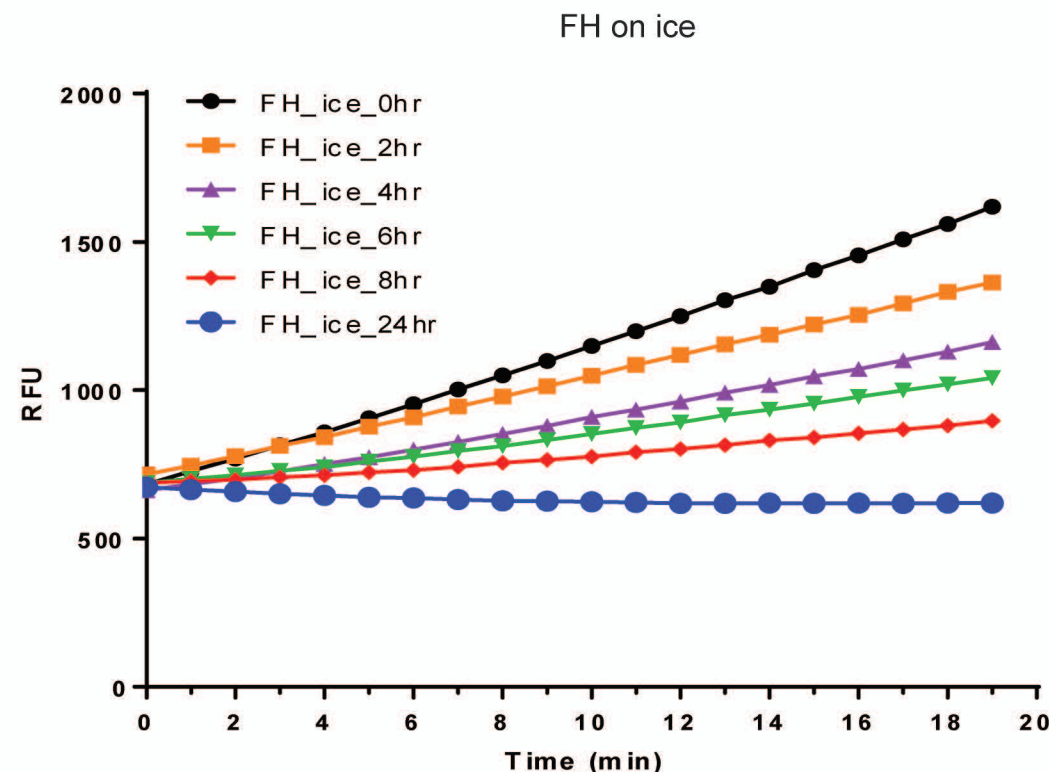


Supplemental figure 1

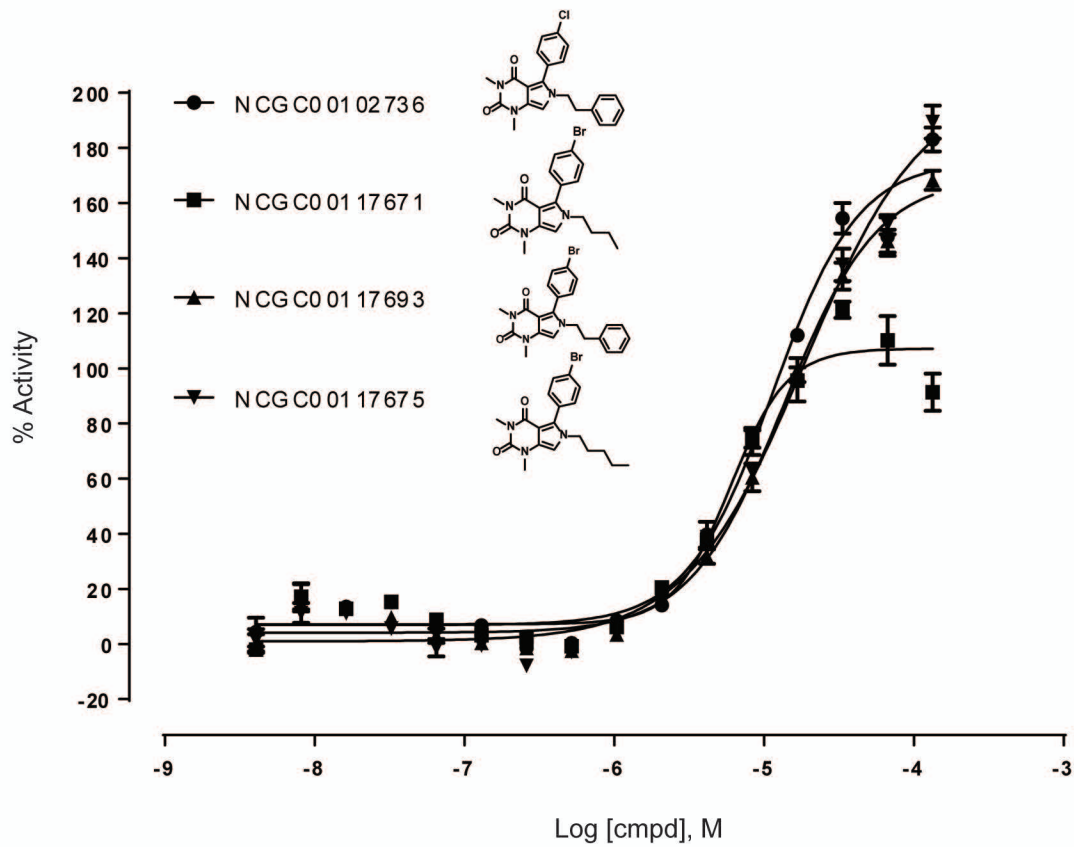
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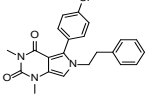
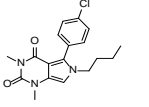
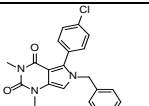
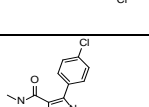
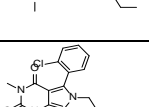
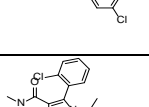
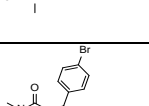
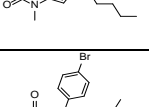
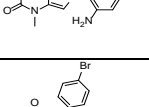
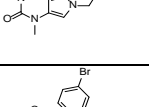
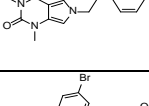
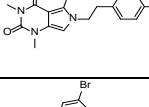
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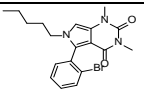
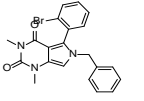
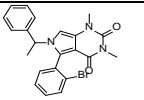
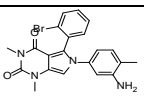
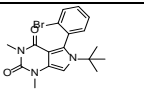
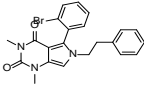
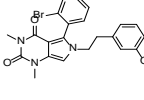
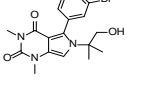
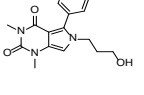


Supplemental figure 2



Supplemental Table 1. Expansion of the series of activators of FH

Sample ID	Library source	Structure	AC50 (uM)	Efficacy (%)	Smiles	Promiscuity score *	Total assay tested
NCGC00102736	Sytravon		8.893	79	<chem>CN1C(=O)N(C)C2=C[N](CCC3=CC=CC=C3)C(=C2C1=O)C4=CC=C(Cl)C=C4</chem>	0.0804	224
NCGC00115662	Sytravon		25.064	60	<chem>CCCC[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=CC=C(Cl)C=C3</chem>	0.0789	228
NCGC00115664	Sytravon		17.744	52	<chem>CN1C(=O)N(C)C2=C[N](CC3=CC=C(Cl)C=C3)C(=C2C1=O)C4=CC=C(Cl)C=C4</chem>	0.0478	209
NCGC00115666	Sytravon		5.611	35	<chem>CCCC[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=CC=C(Cl)C=C3</chem>	0.0439	205
NCGC00115668	Sytravon		15.814	45	<chem>CN1C(=O)N(C)C2=C[N](CC3=CC=C(Cl)C=C3)C(=C2C1=O)C4=C(Cl)C=CC=C4</chem>	0.0392	204
NCGC00115672	Sytravon		null	0	<chem>CC(C)[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=C(Cl)C=CC=C3</chem>	0.0439	228
NCGC00117671	Sytravon		7.926	60	<chem>CCCC[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=CC=C(Br)C=C3</chem>	0.0386	207
NCGC00117673	Sytravon		111.956	-18	<chem>CN1C(=O)N(C)C2=C[N](C3=C(N)C=C(C)C(=C3)C(=C2C1=O)C4=CC=C(Br)C=C4</chem>	0.0435	207
NCGC00117675	Sytravon		9.978	79	<chem>CCCC[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=CC=C(Br)C=C3</chem>	0.0508	256
NCGC00117693	Sytravon		7.064	64	<chem>CN1C(=O)N(C)C2=C[N](CCC3=CC=CC=C3)C(=C2C1=O)C4=CC=C(Br)C=C4</chem>	0.1055	218
NCGC00117695	Sytravon		31.553	79	<chem>COC1=CC=C(C(C[N]2C=C3N(C)C(=O)N(C)C(=O)C3=C2C4=CC=C(Br)C=C4)C=C1OC</chem>	0.0488	205
NCGC00117697	Sytravon		0.018	14	<chem>CN1C(=O)N(C)C2=C[N](CC3=CC=C(F)C=C3)C(=C2C1=O)C4=CC=C(Br)C=C4</chem>	0.1032	252

NCGC00117699	Sytravon		31.553	50	CCCC[N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1 C3=C(Br)C=CC=C3	0.0293	205
NCGC00117701	Sytravon		28.122	78	CN1C(=O)N(C)C2=C[N](CC3=CC=CC=C3)C(=C2C1=O)C4=C(Br)C=CC=C4	0.0639	219
NCGC00117703	Sytravon		39.723	30	CC([N]1C=C2N(C)C(=O)N(C)C(=O)C2=C1C3=CC=CC=C3Br)C4=CC=CC=C4	0.0724	221
NCGC00117707	Sytravon		99.781	-16	CN1C(=O)N(C)C2=C[N](C3=CC=C(C)C(=C3)N)C(=C2C1=O)C4=CC=CC=C4Br	0.0596	218
NCGC00117725	Sytravon		50.009	9	CN1C(=O)N(C)C2=C[N](C(=C2C1=O)C3=CC=CC=C3Br)C(C)(C)C	0.0365	219
NCGC00117727	Sytravon		25.064	70	CN1C(=O)N(C)C2=C[N](CCC3=CC=CC=C3)C(=C2C1=O)C4=CC=CC=C4Br	0.0425	212
NCGC00117729	Sytravon		50.009	24	COC1=C(OC)C=C(CC[N]2C=C3N(C)C(=O)N(C)C(=O)C3=C2C4=CC=CC=C4Br)C=C1	0.0390	205
NCGC00119865	Sytravon		null	0	CN1C(=O)N(C)C2=C[N](C(=C2C1=O)C3=CC(=CC=C3)Br)C(C)(C)CO	0.0153	196
NCGC00141286	Sytravon		0.007	-19	CN1C2=CN(CCCO)C(=C2C(=O)N(C)C1=O)C3=CC=CC=C3	0.0047	212

*Promiscuity score is the general assessment of compound activity profile. It equals to active assays/total assays historically tested in NCATS database. Promiscuity score below 0.15 is considered as non-frequent hitter.