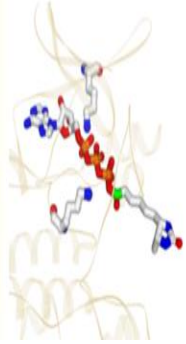
KiNativ® Inhibition Profiles for Selected JAK Inhibitors (Profile in PBMC lysate, ~200 kinases quantitated, only displaying kinases inhibited by at least one inhibitor)



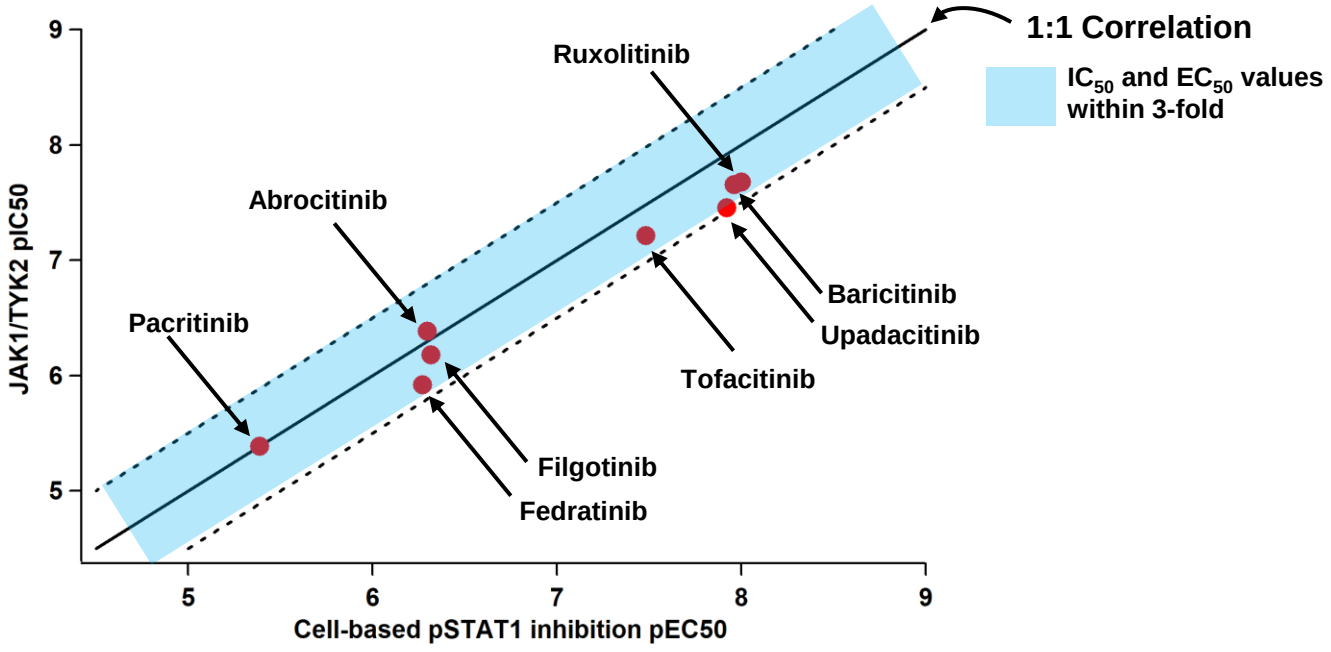
*Clinically approved drugs

Kinase	Ruxolitinib*	Tofacitinib*	Upadacitinib*	Baricitinib*	Fedratinib*	Filgotinib	Pacritinib	Abrocitinib
JAK1 JH1	0.040	0.061	0.035	0.022	1.2	0.66	4.1	0.41
JAK2 JH1	0.030	0.23	0.55	0.043	0.49	2.6	0.85	4.9
JAK3 JH1	0.40	0.10	2.7	1.2	>10	>10	0.58	>10
TYK2 JH1	0.17	0.43	2.4	0.14	9.2	0.35	>10	2.9
JAK1 JH2	>10	>10	>10	>10	0.60	3.9	0.41	>10
AAK1	>10	>10	>10	1.2	>10	>10	>10	>10
ABL, ARG	>10	>10	>10	>10	5.4	5.4	4.1	>10
ACK	1.3	>10	9.0	3.3	0.64	>10	2.0	>10
AMPKa1, AMPKa2	4.0	>10	4.9	8.5	9.3	>10	3.8	>10
BLK	>10	>10	>10	>10	3.8	>10	2.5	>10
BTK	>10	>10	>10	>10	9.7	>10	2.3	>10
CaMK1a	0.94	2.2	1.1	0.53	>10	>10	7.4	2.3
CaMK1d	1.1	3.4	3.0	0.54	>10	>10	>10	6.4
CaMK2a, CaMK2b, CaMK2d, CaMK2g	0.48	8.1	>10	0.95	3.1	>10	7.2	>10
CaMK2d	0.19	4.3	8.2	0.29	1.4	>10	5.9	2.4
CaMK2g	0.17	4.5	3.8	0.23	1.2	>10	2.7	2.6
CaMK4	>10	>10	>10	>10	>10	>10	>10	5.7
CaMKK2	>10	>10	>10	>10	>10	>10	0.75	>10
CASK	1.1	>10	>10	>10	>10	>10	>10	>10
CDK2	>10	>10	>10	>10	>10	>10	9.6	>10
CDK7	>10	>10	>10	>10	5.3	>10	>10	>10
CDK9	>10	>10	>10	>10	>10	>10	1.6	>10
CHK2	>10	>10	>10	4.1	2.0	>10	>10	>10
Erk5	6.3	>10	>10	>10	0.47	>10	>10	>10
FER	>10	>10	>10	>10	4.5	>10	1.4	>10
GCK	>10	>10	>10	>10	>10	>10	4.1	>10
GCN2 domain2	>10	>10	>10	>10	>10	>10	3.1	>10
GSK3A	>10	>10	>10	>10	>10	>10	3.7	>10
HCK	>10	>10	>10	>10	8.4	>10	6.2	>10
HPK1	>10	>10	>10	>10	6.6	>10	6.0	>10
IKKe	2.3	>10	>10	2.8	0.63	6.7	0.79	>10
IKKe, TBK1	2.3	>10	>10	4.3	0.65	3.3	0.77	5.5
ILK	>10	>10	>10	>10	2.9	>10	>10	>10
IRAK1	>10	>10	>10	>10	>10	2.3	0.62	>10
IRAK3	1.5	>10	6.2	>10	0.78	1.8	0.098	>10
JNK1, JNK2, JNK3	>10	>10	>10	>10	0.40	2.9	1.6	>10
LCK	>10	>10	>10	>10	1.5	>10	2.6	>10
LKB1	>10	>10	>10	>10	>10	>10	2.3	>10
LOK	>10	>10	>10	>10	>10	1.7	2.9	>10
LRRK2	6.7	>10	>10	>10	>10	>10	>10	>10
LYN	>10	>10	>10	>10	6.0	>10	6.5	>10
MAP3K1	4.4	1.2	5.1	0.92	>10	>10	>10	>10
MAP3K2	4.0	>10	>10	8.2	>10	>10	>10	>10
MAP3K3	7.8	>10	>10	>10	>10	>10	>10	>10
MARK1, MARK2	5.5	8.0	2.9	1.0	>10	>10	>10	>10
MARK2	2.7	7.0	2.2	1.4	>10	>10	>10	>10
MARK2, MARK3	3.1	>10	3.0	2.3	>10	>10	>10	>10
MARK3	4.8	>10	4.5	2.1	>10	>10	>10	>10
MARK3, MARK4	5.4	>10	3.6	2.8	8.9	>10	>10	>10
MLK3	2.3	>10	>10	>10	4.1	>10	3.6	>10
MPSK1	1.9	>10	>10	6.2	0.043	>10	0.15	8.1
NEK9	1.1	>10	>10	1.1	0.23	3.0	0.32	1.8
NuaK2	>10	6.5	8.8	>10	>10	>10	2.8	>10
p38d, p38g	7.9	>10	>10	>10	6.0	5.3	>10	>10
PIK3C3	4.2	>10	>10	3.3	0.77	9.7	0.35	>10
PIK3CB	>10	>10	>10	>10	>10	>10	5.2	>10
PIK3CD	>10	>10	>10	6.2	7.1	>10	0.045	>10
PIP4K2C	3.9	>10	>10	>10	>10	5.8	0.62	>10
PIP5K3	>10	>10	>10	>10	>10	>10	0.62	>10
PITSLRE	>10	>10	>10	>10	>10	7.3	>10	>10
PKN1	6.0	0.53	>10	2.0	6.0	>10	>10	>10
PKR	>10	>10	>10	>10	5.5	>10	1.1	>10
PYK2	1.7	>10	7.1	>10	1.5	>10	4.8	>10
ROCK1	4.0	>10	>10	9.7	>10	>10	>10	>10
ROCK1, ROCK2	5.6	>10	>10	>10	>10	>10	>10	>10
RSK1 domain1	>10	>10	>10	>10	4.2	>10	3.8	>10
RSK1 domain1, RSK2 domain1, RSK3 domain1	>10	>10	>10	>10	3.7	>10	>10	>10
RSK1 domain2	0.42	0.96	>10	0.39	9.8	>10	>10	>10
RSK2 domain1	>10	>10	>10	>10	7.3	>10	>10	>10
RSK2 domain2	3.1	2.1	>10	1.9	>10	>10	>10	>10
SLK	>10	>10	>10	>10	>10	6.5	3.3	>10
TAO2	2.7	>10	>10	6.4	>10	>10	7.9	>10
TBK1	2.3	9.2	>10	6.4	0.39	1.4	0.92	6.9
ULK3	>10	>10	>10	>10	9.4	>10	>10	>10
ZAK	>10	>10	>10	>10	>10	>10	4.3	>10
ZC1/HGK, ZC2/TNIK, ZC3/MINK	>10	>10	>10	>10	>10	>10	0.96	>10
ZC2/TNIK	>10	>10	>10	>10	>10	>10	0.43	>10

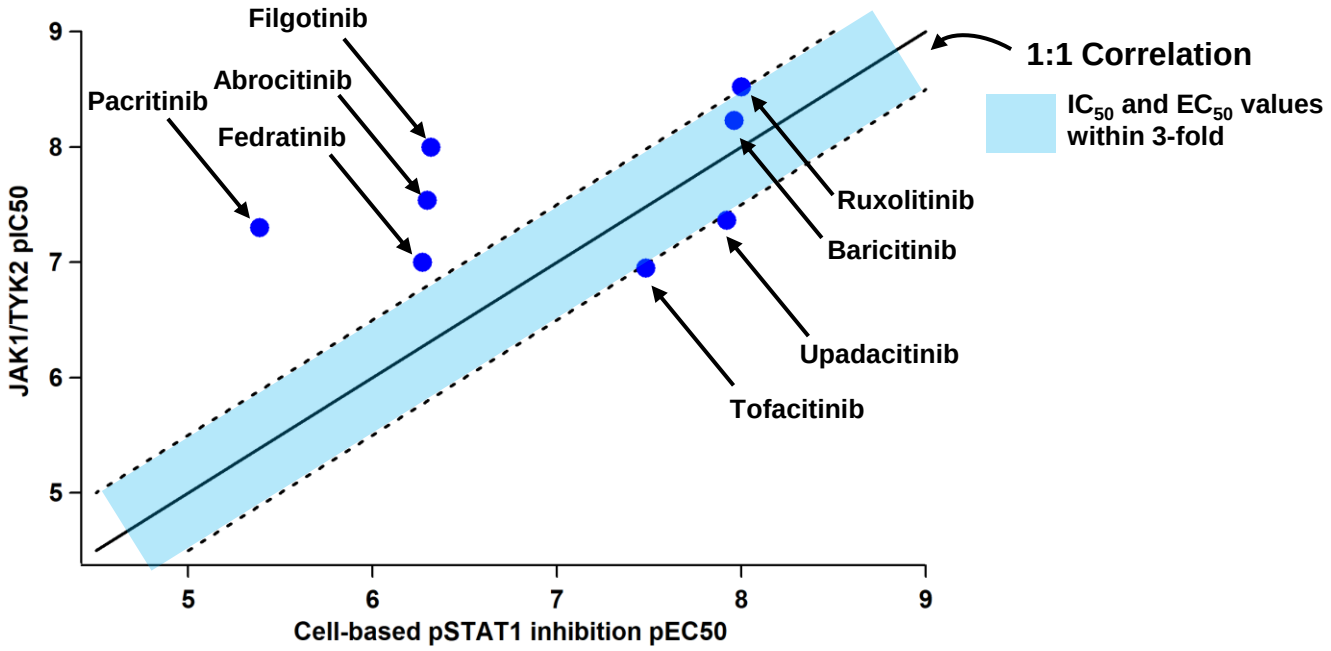
IC_{50} (μM)
<0.05
0.05-0.25
0.25-1.25
1.25-10
>10

IC_{50} values determined by KiNativ correlate with EC_{50} values from a cell-based assay significantly better than IC_{50} values determined by profiling against the recombinant kinases

KiNativ IC_{50} values versus cell-based EC_{50} values



Recombinant kinase IC_{50} values versus cell-based EC_{50} values



Cell based assay: Monitor inhibition of INFα dependent pSTAT1 phosphorylation in Jurkat, driven by JAK1:TYK2 heterodimer