CARNA BIOSCIENCES

Designed for Compounds with Slow Binding Kinetics

Preincubation Kinase Profiling Service

Available for **165** Kinases*

Preincubation Assay is now available from Carna!

Certain classes of kinase inhibitors exhibit slow binding kinetics as shown in Figure1.

For such compounds, preincubation (Figure 2) is necessary to assess their maximal effect (Figure 3 and 4).

We are pleased to announce a new kinase profiling service that incorporates preincubation with the test compound(s). A thirty (30) minute preincubation at room temperature is typically sufficient to capture such slow binding compounds, after which their activity is evaluated using our standard Mobility Shift Assay.

This service is specifically designed to measure compounds with slow association kinetics, and the corresponding studies are conducted once per month. Please inquire for more detailed information.

* As of June 30, 2014

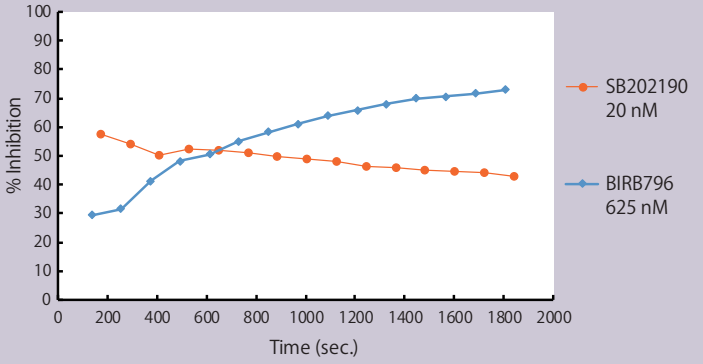


Fig. 1 Time course of p38α inhibitors

Structurally unrelated SB202190 and BIRB796 are potent inhibitors of p38α. BIRB796 interacts with p38α in a manner different from SB202190, and its binding induces a slow conformational change that locks the protein into an inactive conformation. Therefore, the potency of BIRB796 increased with the period of incubation.
The assay was performed at an ATP concentration of 1mM.

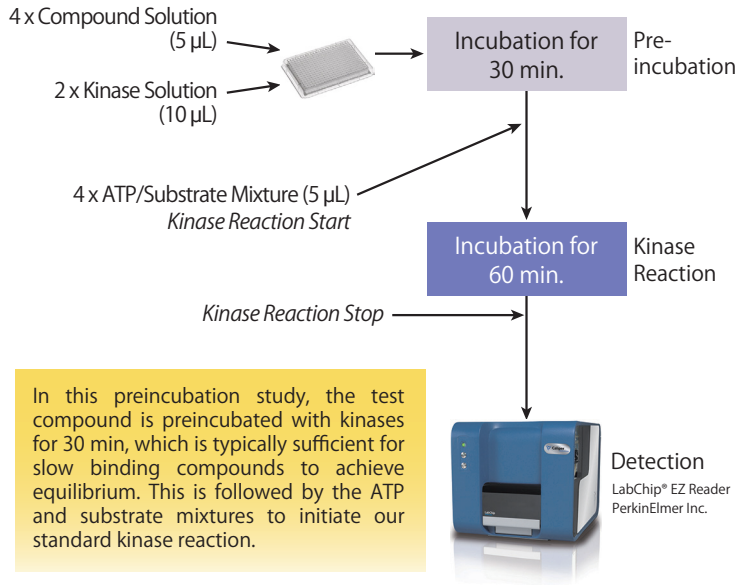
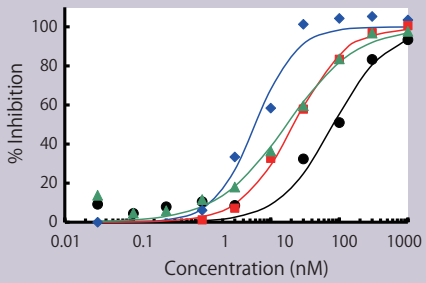


Fig. 2 Preincubation Study Methodology



	Preincubation	
	+	−
BIRB796	9.5 (◆)	82 (●)
SB202190	19 (▲)	22 (■)

Fig. 3 IC50 Comparison with or without Preincubation for p38α Inhibitors

Preincubation did not affect the IC50 of SB202190, however, a significant change was observed for the activity of BIRB796.
The assay was performed at an ATP concentration of 1mM.

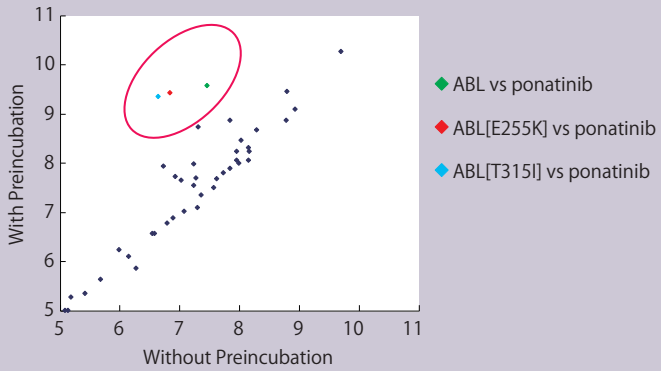


Fig. 4 IC50 Comparison with or without Preincubation for Clinical Inhibitors

Several clinical kinase inhibitors and their corresponding target kinases were evaluated in a preincubation study; the resulting pIC50 values are compared above. In most cases, good correlations were observed. However, Ponatinib showed enhanced inhibition of native and mutant isoforms of the ABL kinase following preincubation. All assays were performed at an ATP concentration of 1mM.

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QuickScout™ Custom Profiling from Carna Biosciences, Inc.

Preincubation

This profiling service incorporates a 30 minute preincubation at room temperature with the test compound(s).
You may select an individual kinase or group of kinases from the list below for preincubation profiling.
For more detailed information about the service, please refer to the latest "Kinase Profiling Book."

Tyrosine Kinases
ABL(ABL1)
ABL(ABL1) [E255K]
ABL(ABL1) [T315I]
ALK
ALK [F1174L]
ALK [L1196M]
ALK [R1275Q]
ARG(ABL2)
BMX
EGFR(ERBB1)
EGFR(ERBB1) [d746-750]
EGFR(ERBB1) [d746-750/T790M]
EGFR(ERBB1) [L858R]
EGFR(ERBB1) [L861Q]
EGFR(ERBB1) [T790M]
EGFR(ERBB1) [T790M/L858R]
EPHA1
EPHA2
EPHA3
EPHA4
EPHA5
EPHA6
EPHA7
EPHA8
EPHB1
EPHB2
EPHB3
EPHB4
FER
FES
FGFR1
FGFR2
FGFR4
FGFR4 [V550L]
FGR
FLT1
FLT4
FRK
HER4(ERBB4)
IGF1R
INSR
JAK2
JAK3
KDR
LCK
LYNa
LYNb
MER(MERTK)
MET
MET [D1228H]
MET [M1250T]
MET [Y1235D]
NPM1-ALK
PYK2(PTK2B)
RET
RET [G691S]
RET [M918T]
RET [S891A]
RET [Y791F]

Tyrosine Kinases
RON(MST1R)
ROS(ROS1)
SRC
SRM(SRMS)
TEC
TIE2(TEK)
TRKB(NTRK2)
TRKC(NTRK3)
TYRO3
YES(YES1)
YES(YES1) [T348I]

Serine/Threonine Kinases
AKT1
AKT2
AKT3
AMPKα1/β1/γ1(PRKAA1/B1/G1)
AMPKα2/β1/γ1(PRKAA2/B1/G1)
AurA(AURKA)
AurA(AURKA)/TPX2
AurB(AURKB)/INCENP
BRSK1
BRSK2
CaMK2α(CAMK2A)
CaMK2β(CAMK2B)
CaMK2γ(CAMK2G)
CaMK2δ(CAMK2D)
CaMK4
CDC2(CDK1)/CycB1
CDK2/CycA2
CDK2/CycE1
CDK3/CycE1
CDK5/p25
CGK2(PRKG2)
CHK1(CHEK1)
CHK2(CHEK2)
CK1γ1(CSNK1G1)
CK1γ2(CSNK1G2)
CK1γ3(CSNK1G3)
CK1δ(CSNK1D)
CK2α1(CSNK2A1)/β
CK2α2(CSNK2A2)/β
CLK1
CLK2
CLK3
DAPK1
DYRK1A
DYRK1B
DYRK2
DYRK3
Erk1(MAPK3)
Erk2(MAPK1)
GSK3α
GSK3β
Haspin(GSG2)
HIPK1
HIPK2
HIPK3

Serine/Threonine Kinases
HIPK4
IKKβ(IKBKB)
JNK1(MAPK8)
JNK2(MAPK9)
JNK3(MAPK10)
MAPKAPK2
MAPKAPK3
MAPKAPK5
MARK1
MARK2
MARK3
MARK4
MGC42105
MNK1(MKNK1)
MNK2(MKNK2)
MSK1(RPS6KA5)
NEK2
NEK4
Nuak1
Nuak2
p38α(MAPK14)
p38β(MAPK11)
p38γ(MAPK12)
p38δ(MAPK13)
p70S6K(RPS6KB1)
p70S6Kβ(RPS6KB2)
PAK1
PAK2
PAK5(PAK7)
PDGFRα(PDGFRA)
PDGFRα(PDGFRA) [V561D]
PDGFRβ(PDGFRB)
PIM1
PKCδ(PRKCD)
PKCε(PRKCE)
PKCζ(PRKCZ)
PKCη(PRKCH)
PKD1(PRKD1)
PKD2(PRKD2)
QIK(SIK2)
ROCK2
RSK2(RPS6KA3)
RSK3(RPS6KA2)
RSK4(RPS6KA6)
SGK
SGK3(SGKL)
skMLCK(MYLK2)
TBK1
TSSK1

Lipid Kinase
SPHK1

Tyrosine Kinases 70
Serine/Threonine Kinases 94
Lipid Kinase 1
Total 165 targets

Updated: 2014/6/30
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