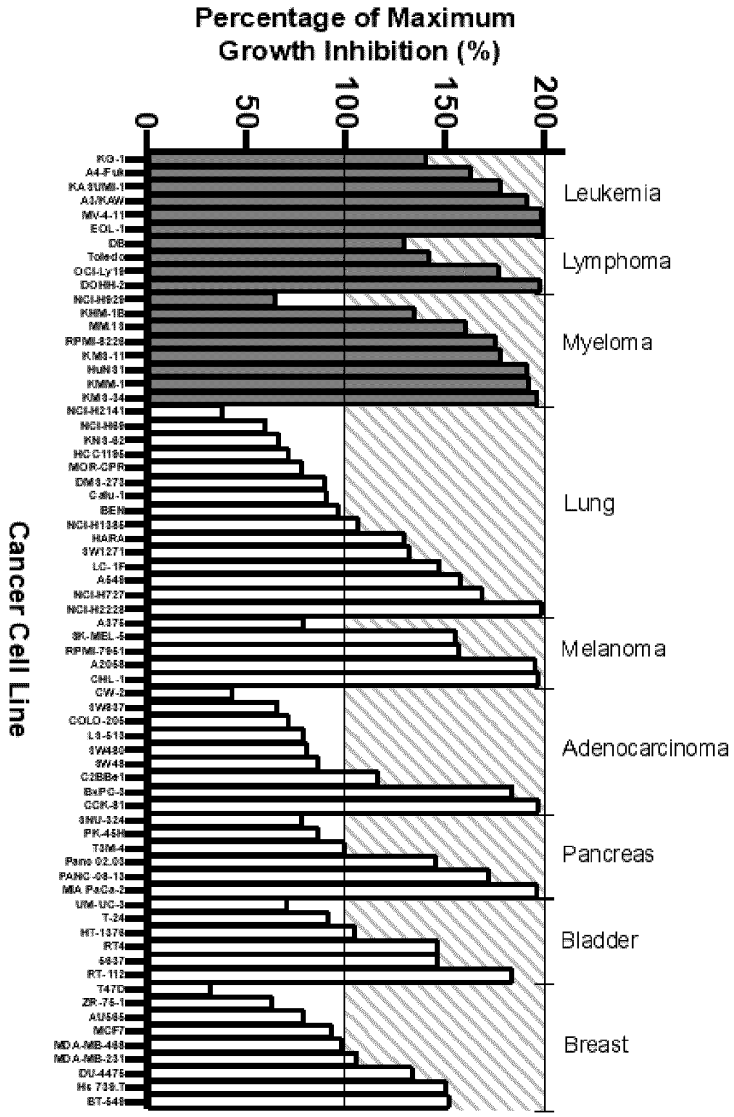

Percentage of Maximum
Growth Inhibition (%)
0
50
100
150
200
Cancer Cell Line
Leukemia
Lymphoma
Myeloma
Lung
Melanoma
Adenocarcinoma
Pancreas
Bladder
Breast

FIG. 1A

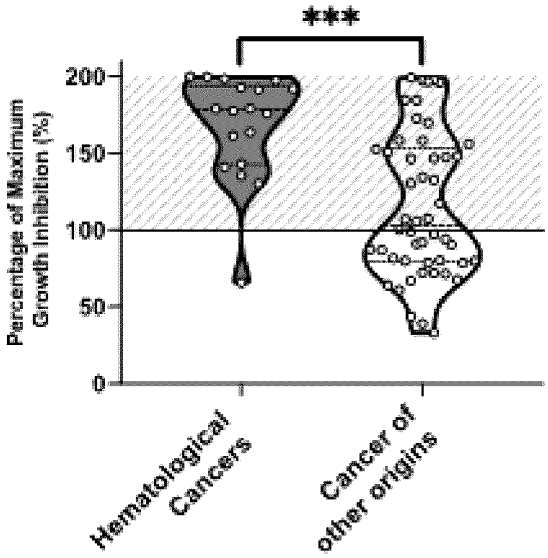

***
200
150
100
50
0
Percentage of Maximum Growth Inhibition (%)
Hematological Cancers
Cancer of other origins

FIG. 1B

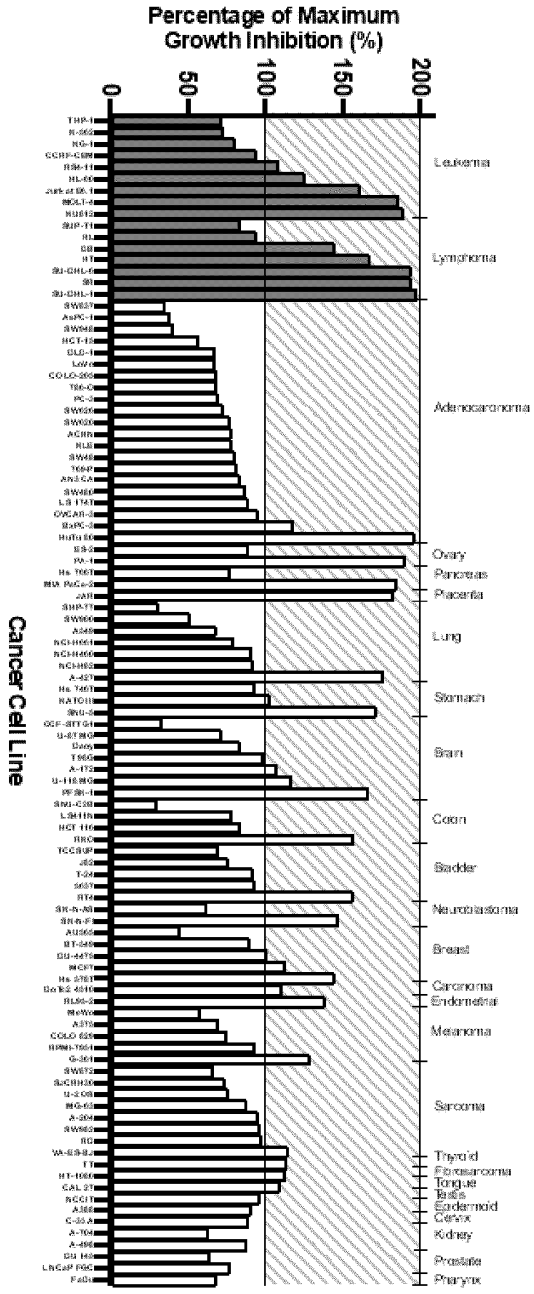

Percentage of Maximum Growth Inhibition (%)
0
50
100
150
200
Cancer Cell Line
Leukemia
Lymphoma
Adenocarcinoma
Ovary
Pancreas
Placenta
Lung
Stomach
Brain
Colon
Bladder
Neuroblastoma
Breast
Carcinoma
Endometria
Melanoma
Sarcoma
Thyroid
Fibrosarcoma
Tongue
Testis
Epidermoid
Cervix
Kidney
Prostate
Pharynx

FIG. 1C

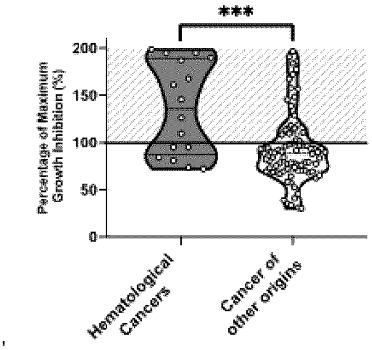


FIG. 1D

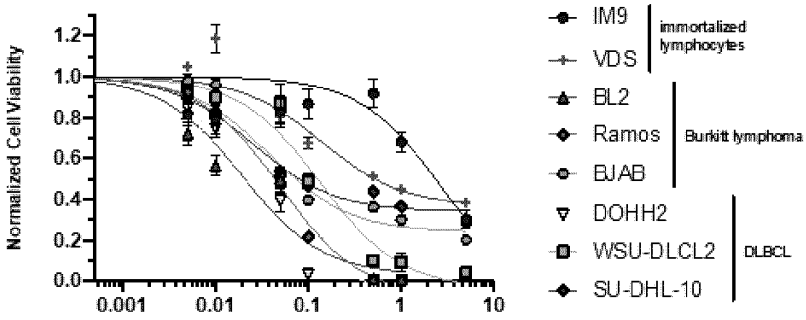


FIG. 1E

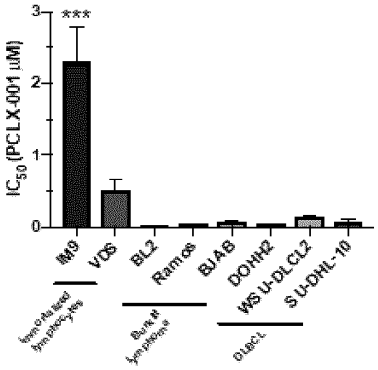


FIG. 1F

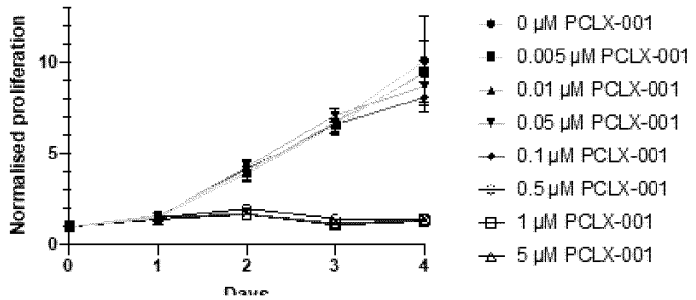

Normalised proliferation
10
5
0
0
1
2
3
4
Days
0 µM PCLX-001
0.005 µM PCLX-001
0.01 µM PCLX-001
0.05 µM PCLX-001
0.1 µM PCLX-001
0.5 µM PCLX-001
1 µM PCLX-001
5 µM PCLX-001

FIG. 1G

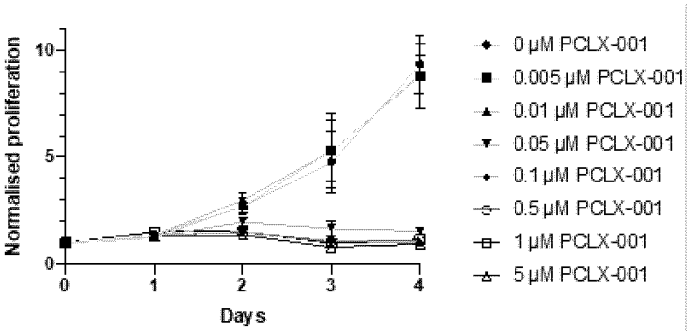

Normalised proliferation
10
5
0
0
1
2
3
4
Days
0 µM PCLX-001
0.005 µM PCLX-001
0.01 µM PCLX-001
0.05 µM PCLX-001
0.1 µM PCLX-001
0.5 µM PCLX-001
1 µM PCLX-001
5 µM PCLX-001

FIG. 1H

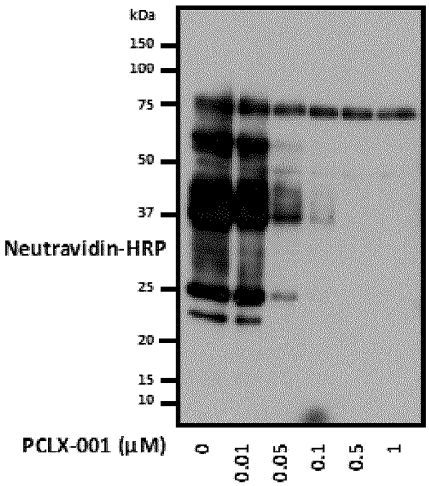

kDa
150
100
75
50
37
Neutravidin-HRP
25
20
15
10
PCLX-001 (µM)
0
0.01
0.05
0.1
0.5
1

FIG. 2A

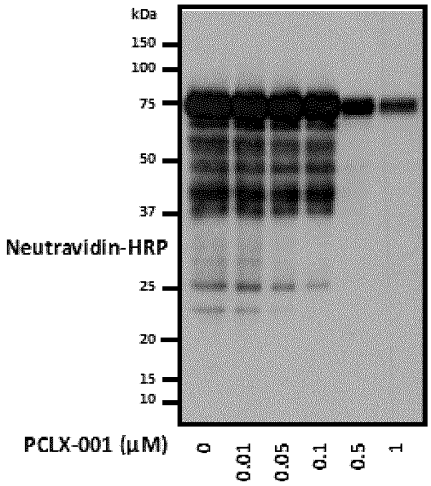

kDa
150
100
75
50
37
Neutravidin-HRP
25
20
15
10
PCLX-001 (µM)
0
0.01
0.05
0.1
0.5
1

FIG. 2B

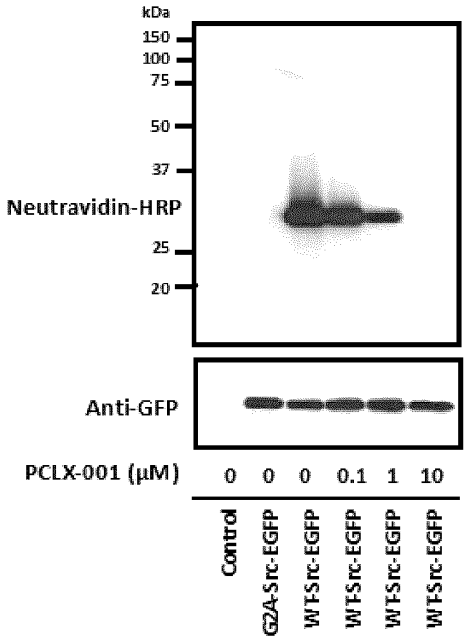

kDa
150
100
75
50
37
Neutravidin-HRP
25
20
Anti-GFP
PCLX-001 (μM)
0 0 0 0.1 1 10
Control
G2A-Src-EGFP
WTSrc-EGFP
WTSrc-EGFP
WTSrc-EGFP
WTSrc-EGFP

FIG. 2C

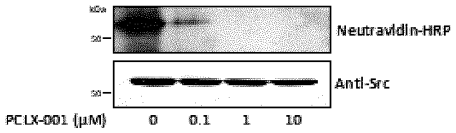

kDa
50
Neutravidin-HRP
50
Anti-Src
PCLX-001 (μM)
0 0.1 1 10

FIG. 2D

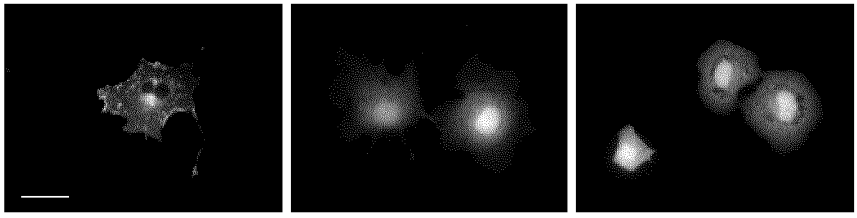


FIG. 2E

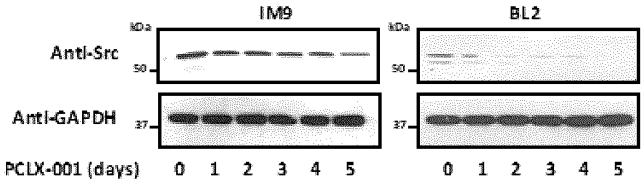


FIG. 2F

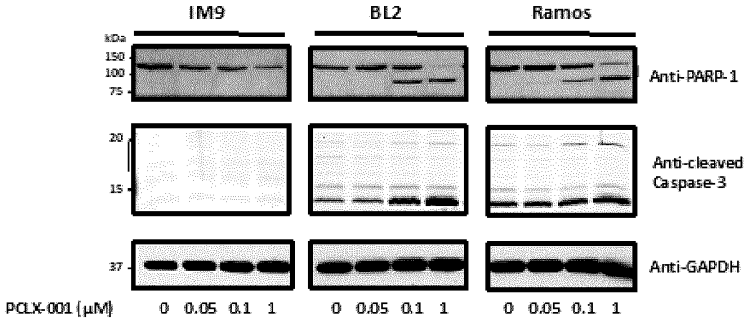


FIG. 2G

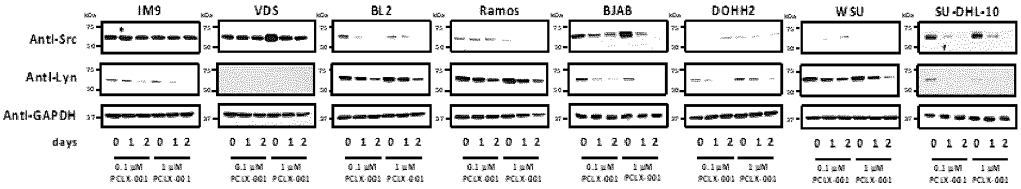

IM9
VDS
BL2
Ramos
BJAB
DOHH2
WSU
SU-DHL-10
Anti-Src
Anti-Lyn
Anti-GAPDH
days
0 1 2 0 1 2
0.1 μM PCLX-001
1 μM PCLX-001

FIG. 3A

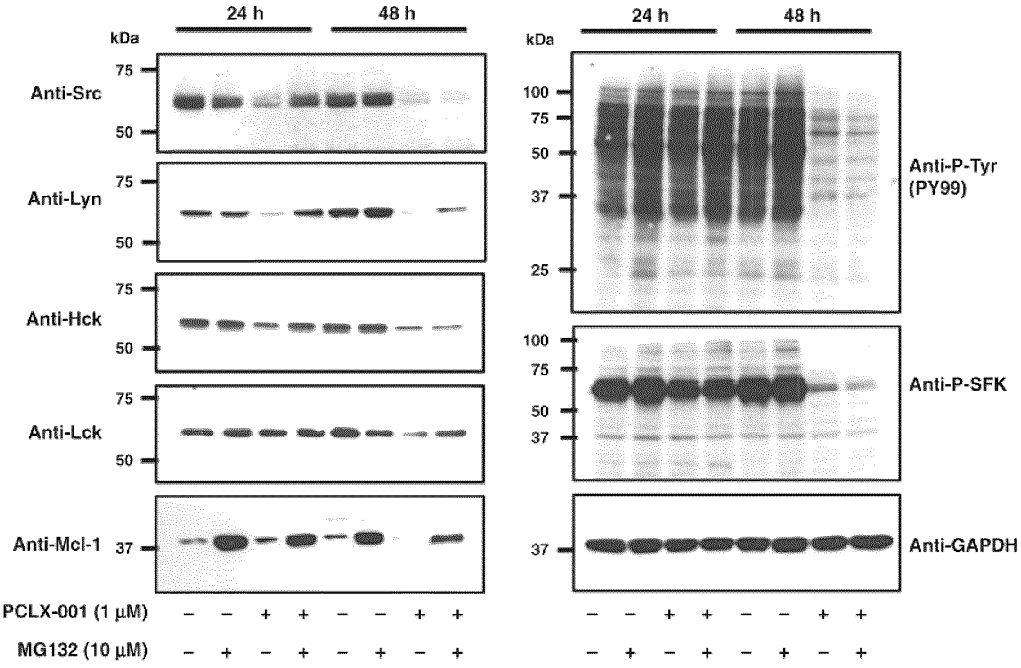

24 h
48 h
kDa
Anti-Src
Anti-Lyn
Anti-Hck
Anti-Lck
Anti-Mcl-1
Anti-P-Tyr (PY99)
Anti-P-SFK
Anti-GAPDH
PCLX-001 (1 μM)
MG132 (10 μM)

FIG. 3B

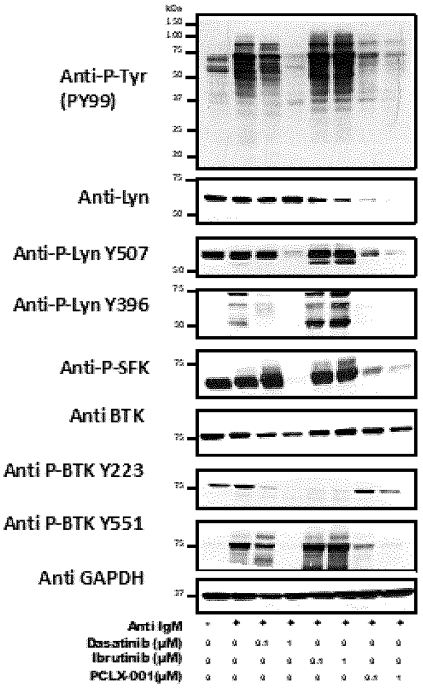

Anti-P-Tyr (PY99)
Anti-Lyn
Anti-P-Lyn Y507
Anti-P-Lyn Y396
Anti-P-SFK
Anti BTK
Anti P-BTK Y223
Anti P-BTK Y551
Anti GAPDH
Anti IgM
Dasatinib (μM)
Ibrutinib (μM)
PCLX-001(μM)

FIG. 4A

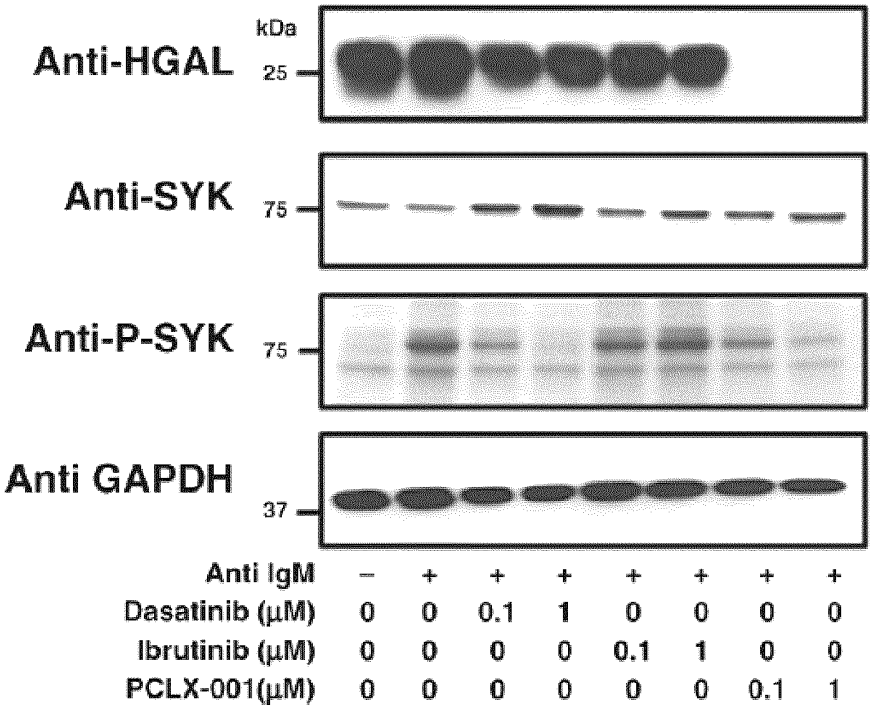

kDa
Anti-HGAL
25
Anti-SYK
75
Anti-P-SYK
75
Anti GAPDH
37
Anti IgM – + + + + + + +
Dasatinib (μM) 0 0 0.1 1 0 0 0 0
Ibrutinib (μM) 0 0 0 0 0.1 1 0 0
PCLX-001(μM) 0 0 0 0 0 0 0.1 1

FIG. 4B

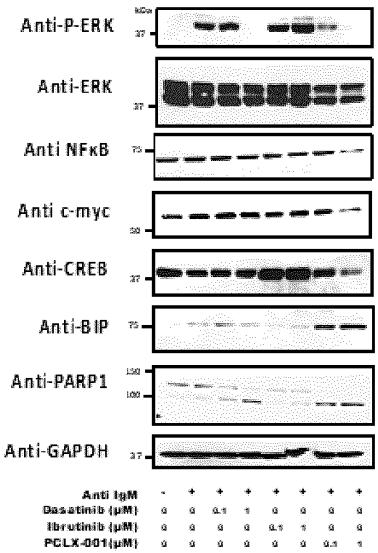

Anti-P-ERK
Anti-ERK
Anti NFκB
Anti c-myc
Anti-CREB
Anti-BIP
Anti-PARP1
Anti-GAPDH
Anti IgM
Dasatinib (μM)
Ibrutinib (μM)
PCLX-001(μM)

FIG. 4C

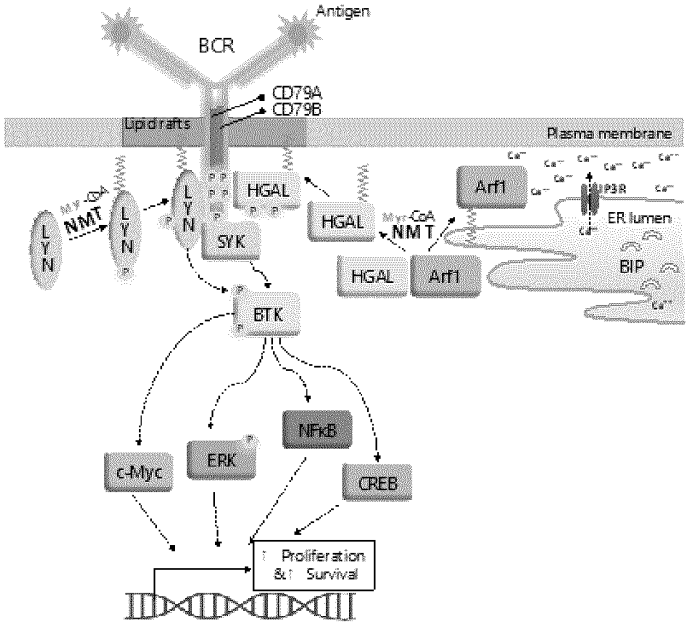

Antigen
BCR
CD79A
CD79B
Lipid rafts
Plasma membrane
LYN
NMT
Myr-CoA
HGAL
SYK
BTK
Arf1
IP3R
ER lumen
BIP
NFκB
ERK
c-Myc
CREB
↑ Proliferation
&↑ Survival

FIG. 5A

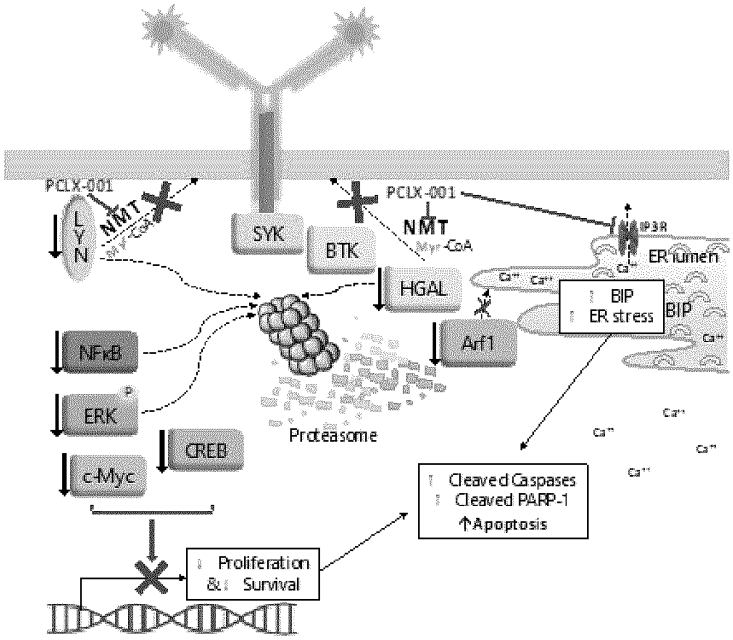

PCLX-001
NMT
Myr-CoA
LYN
SYK
BTK
PCLX-001
NMT
Myr-CoA
IP3R
ER lumen
HGAL
BIP
ER stress
BIP
Arf1
NFκB
ERK
CREB
c-Myc
Proteasome
Cleaved Caspases
Cleaved PARP-1
↑Apoptosis
Proliferation
& Survival

FIG. 5B

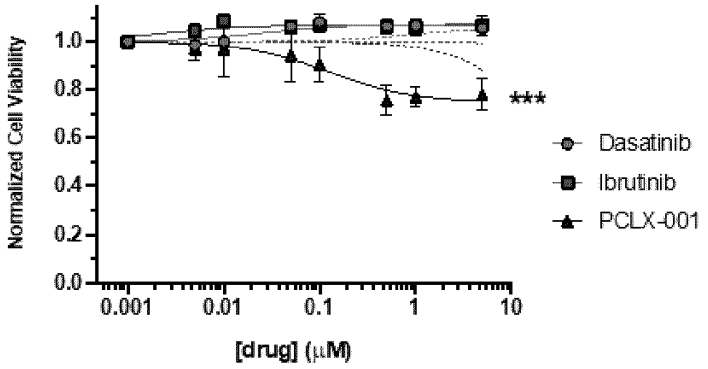

Normalized Cell Viability
1.0
0.8
0.6
0.4
0.2
0.0
0.001
0.01
0.1
1
10
[drug] (μM)
***
Dasatinib
Ibrutinib
PCLX-001

FIG. 6A

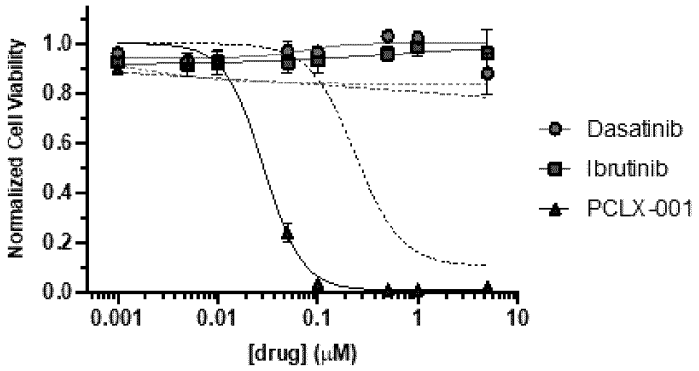

Normalized Cell Viability
1.0
0.8
0.6
0.4
0.2
0.0
0.001
0.01
0.1
1
10
[drug] (μM)
Dasatinib
Ibrutinib
PCLX-001

FIG. 6B

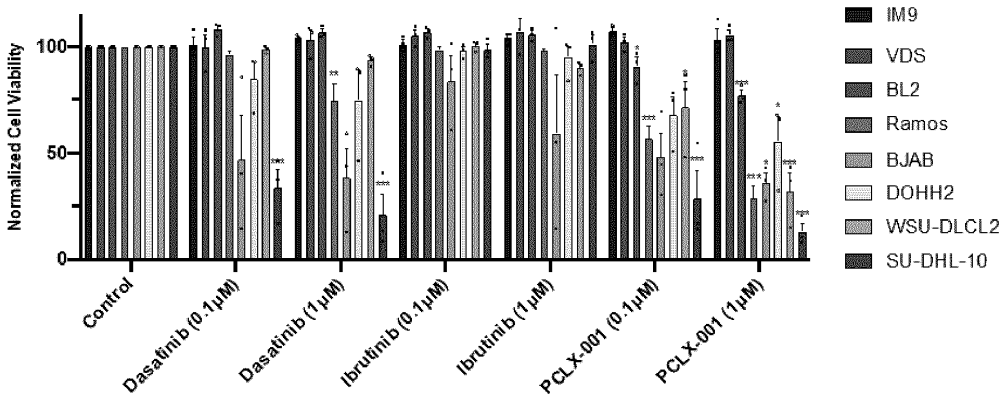

Normalized Cell Viability
100
50
0
Control
Dasatinib (0.1μM)
Dasatinib (1μM)
Ibrutinib (0.1μM)
Ibrutinib (1μM)
PCLX-001 (0.1μM)
PCLX-001 (1μM)
IM9
VDS
BL2
Ramos
BJAB
DOHH2
WSU-DLCL2
SU-DHL-10

FIG. 6C

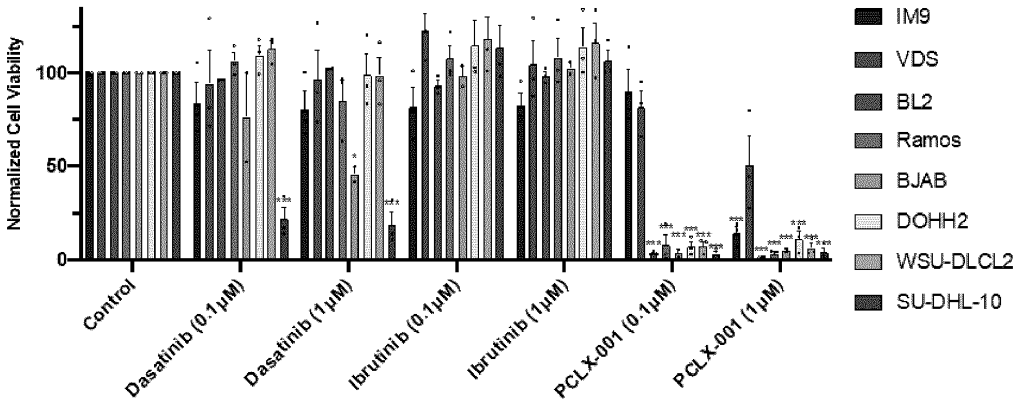


FIG. 6D

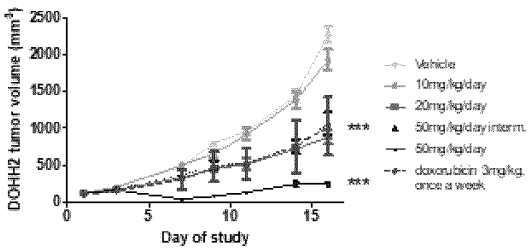


FIG. 7A

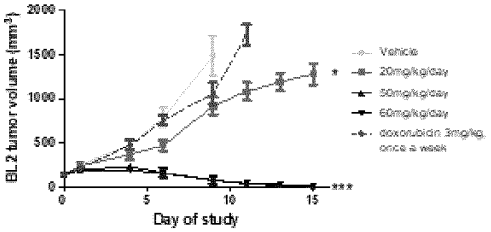


FIG. 7B

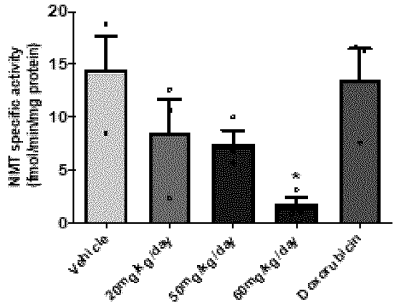


FIG. 7C

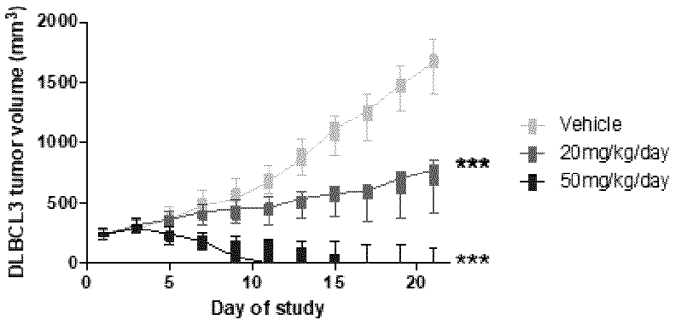


FIG. 7D

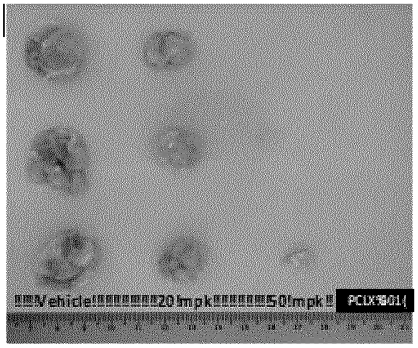


FIG. 7E

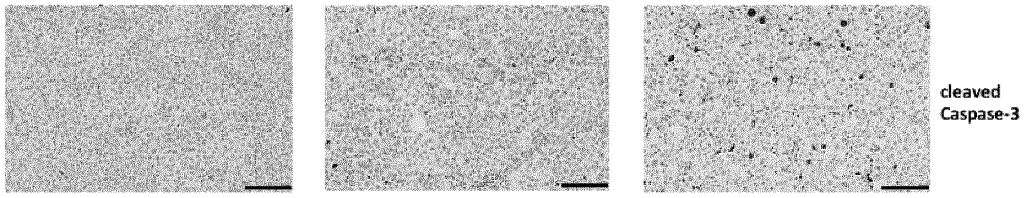

cleaved
Caspase-3
Vehicle
PCLX-001 (20mg/kg/day)
PCLX-001 (50mg/kg/day)

FIG. 7F

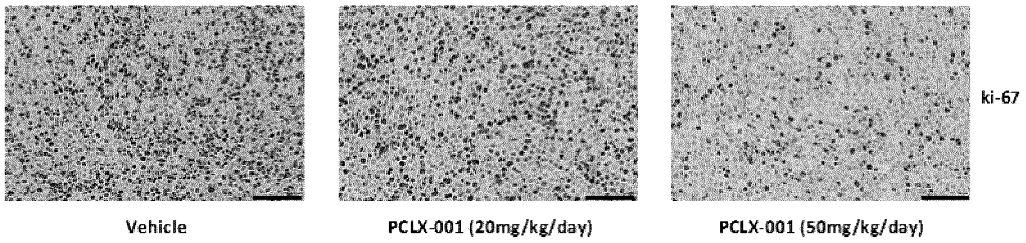

ki-67
Vehicle
PCLX-001 (20mg/kg/day)
PCLX-001 (50mg/kg/day)

FIG. 7G

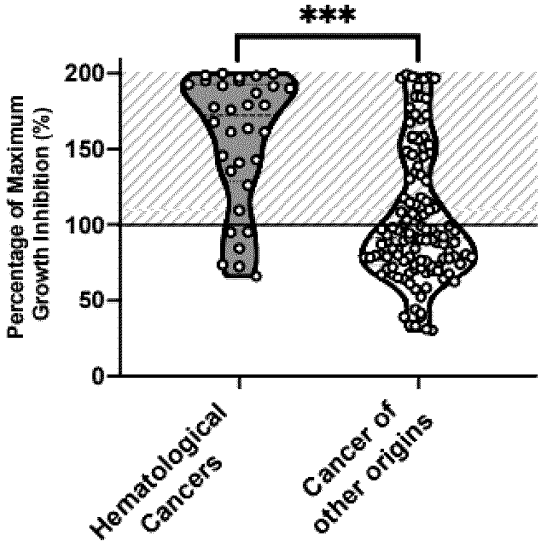

***
200
150
100
50
0
Percentage of Maximum Growth Inhibition (%)
Hematological Cancers
Cancer of other origins

FIG. 8

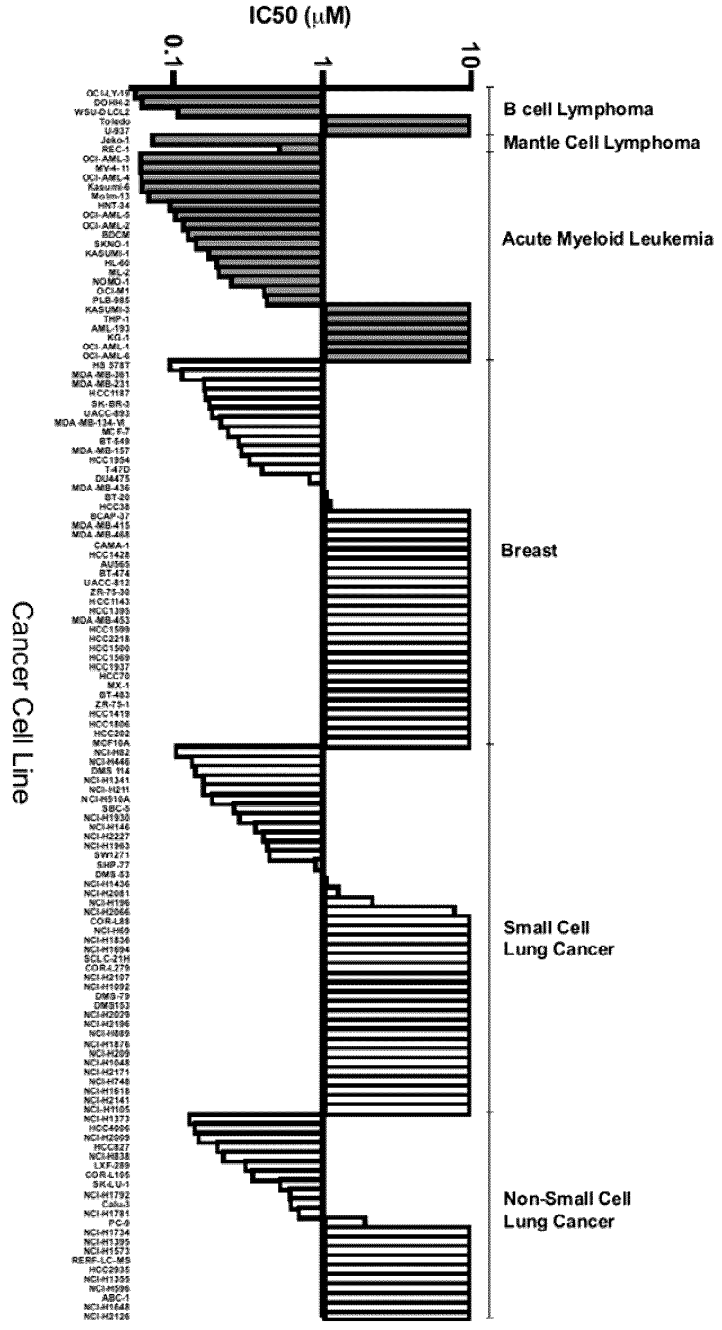

IC50 (μM)
0.1
1
10
Cancer Cell Line
B cell Lymphoma
Mantle Cell Lymphoma
Acute Myeloid Leukemia
Breast
Small Cell
Lung Cancer
Non-Small Cell
Lung Cancer

FIG. 9A

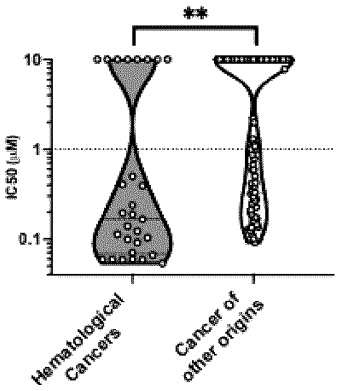

**
10
1
0.1
IC50 (μM)
Hematological Cancers
Cancer of other origins

FIG. 9B

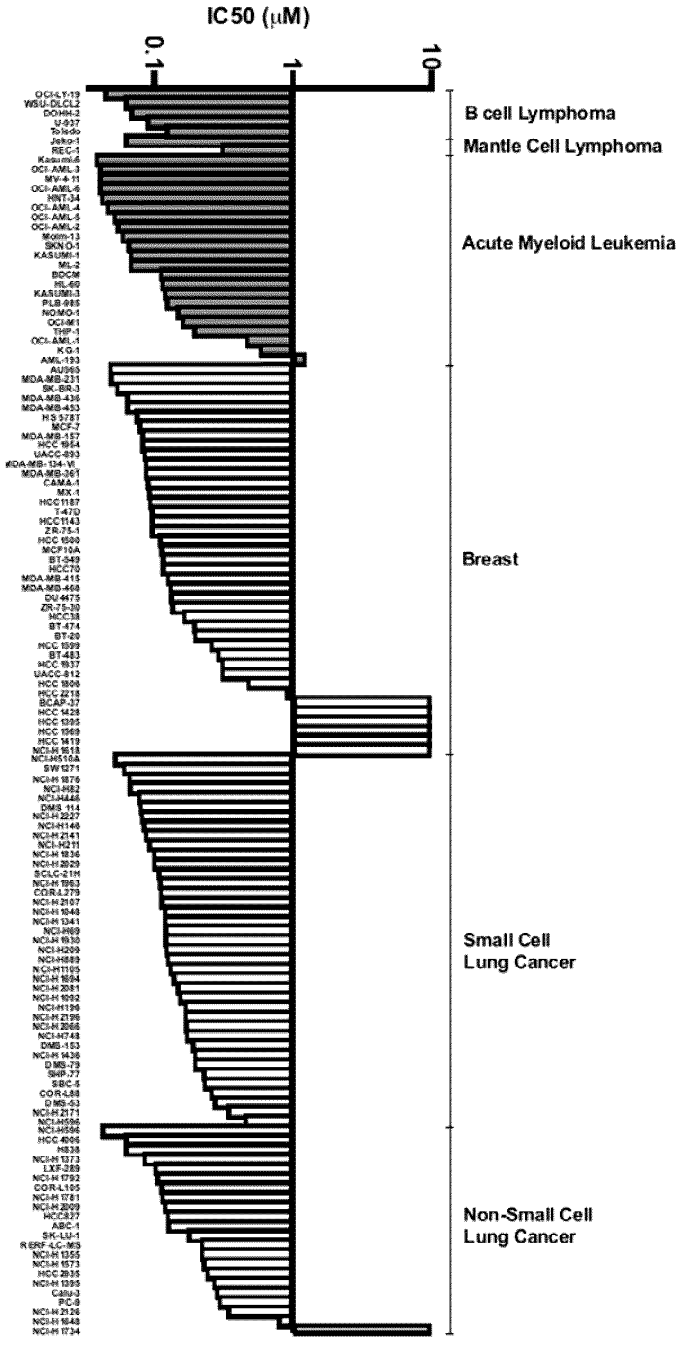

IC50 (μM)
0.1
1
10
B cell Lymphoma
Mantle Cell Lymphoma
Acute Myeloid Leukemia
Breast
Small Cell
Lung Cancer
Non-Small Cell
Lung Cancer

FIG. 9C

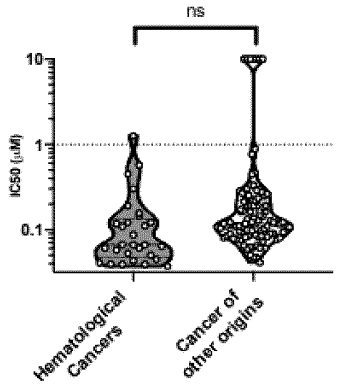


FIG. 9D

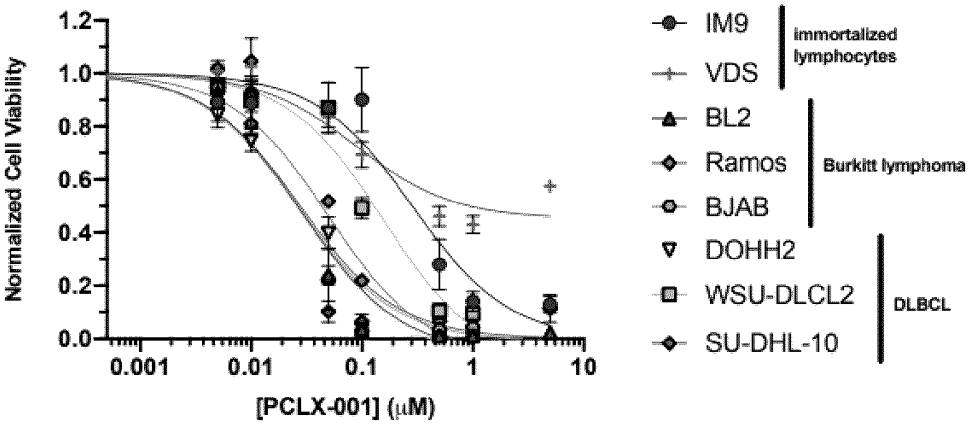


FIG. 10A

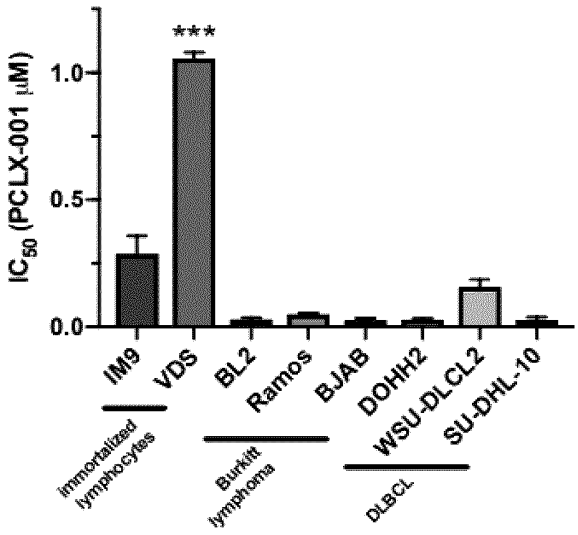

***
1.0
0.5
0.0
IC50 (PCLX-001 μM)
IM9
VDS
BL2
Ramos
BJAB
DOHH2
WSU-DLCL2
SU-DHL-10
immortalized lymphocytes
Burkitt lymphoma
DLBCL

FIG. 10B

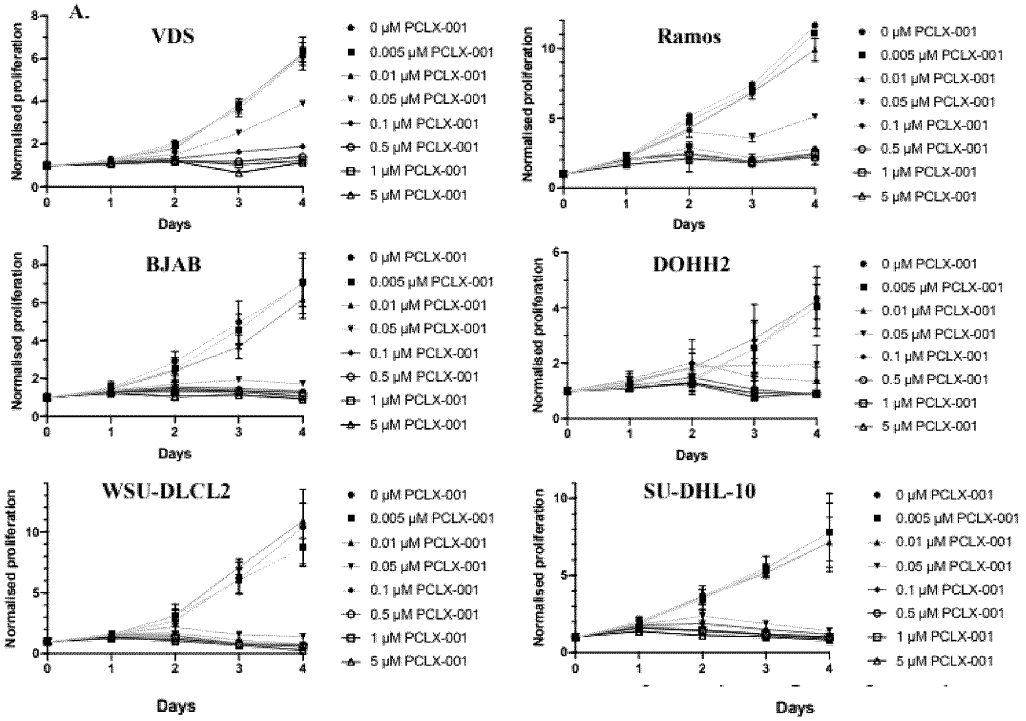


FIG. 11A

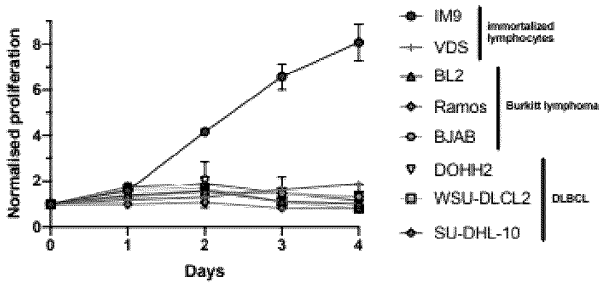


FIG. 11B

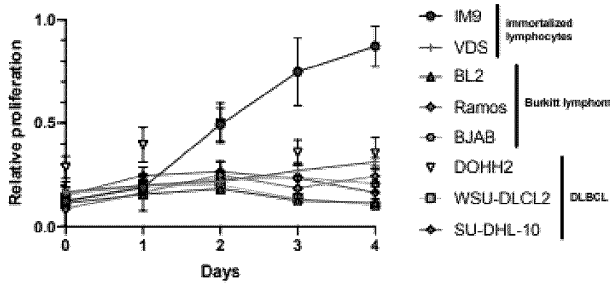


FIG. 11C

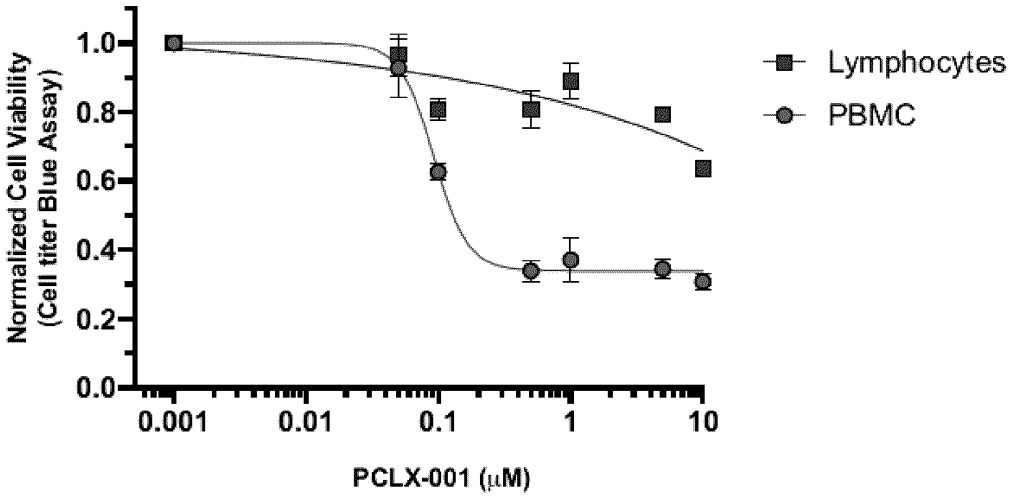


FIG. 12A

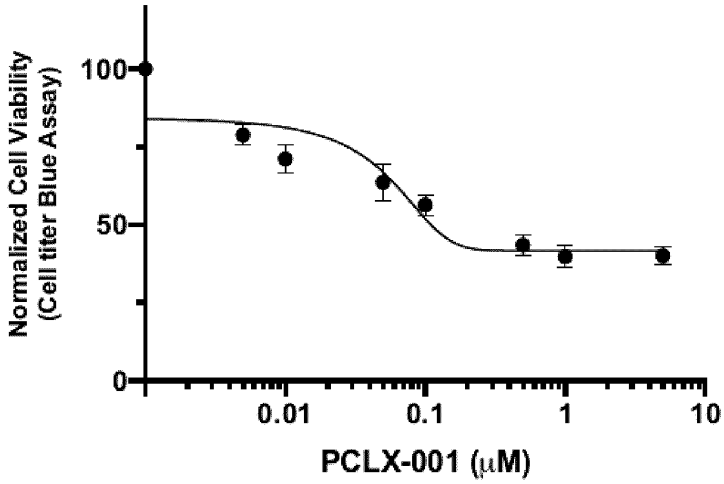


FIG. 12B

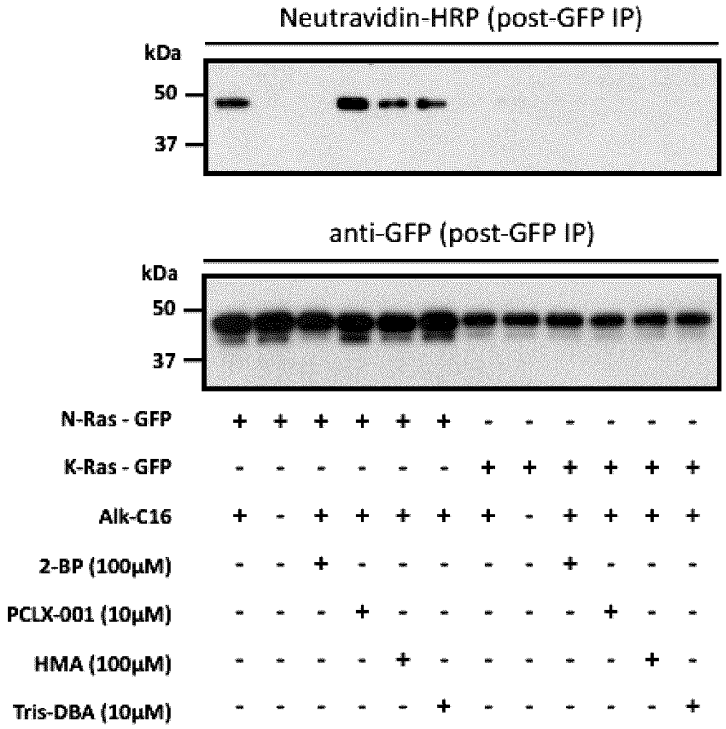


FIG. 13A

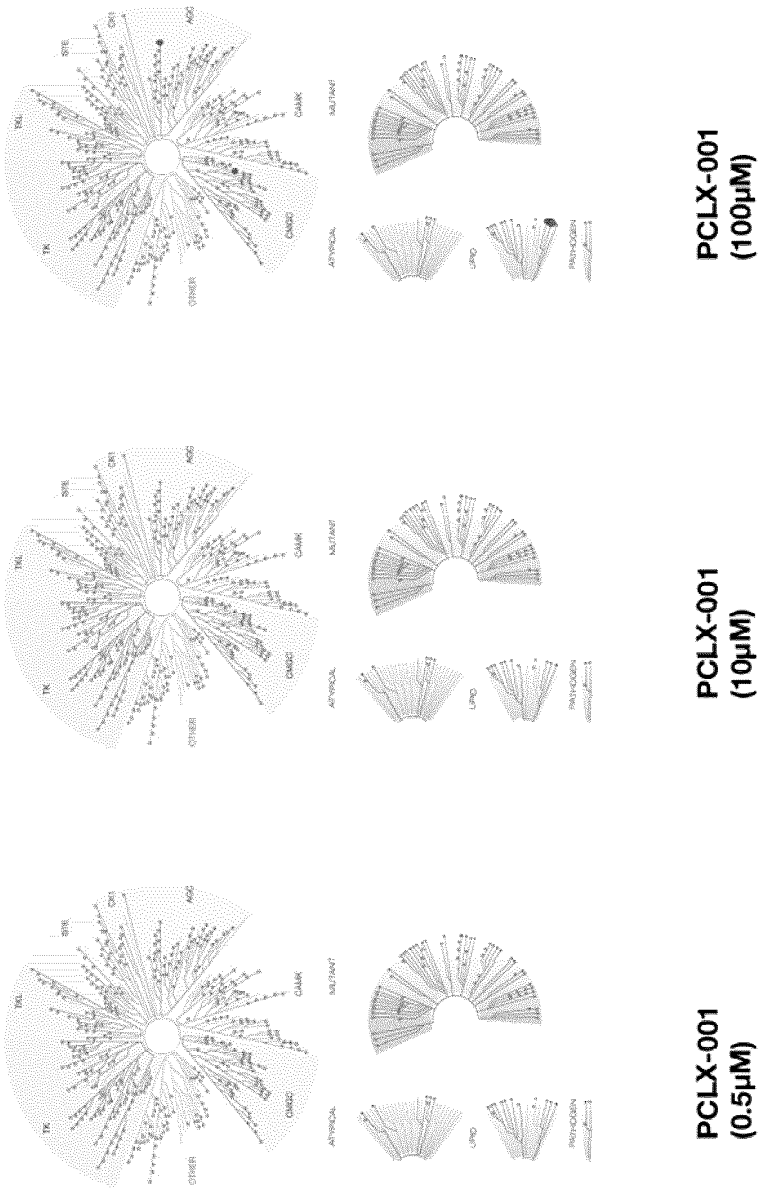


FIG. 13B

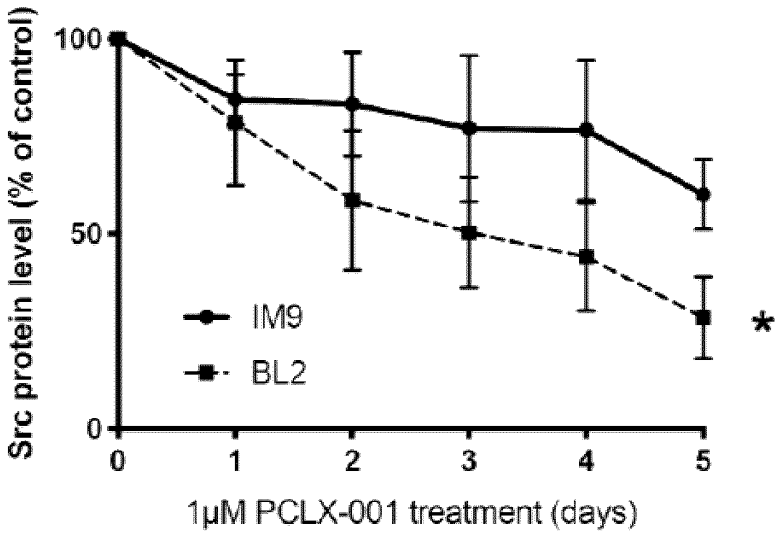


FIG. 14

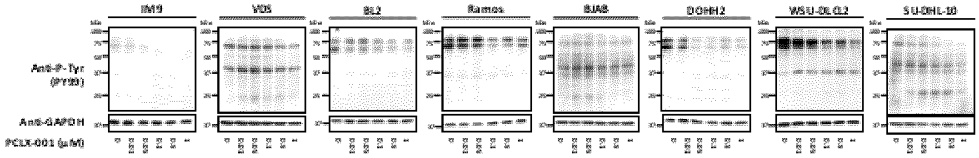


FIG. 15A

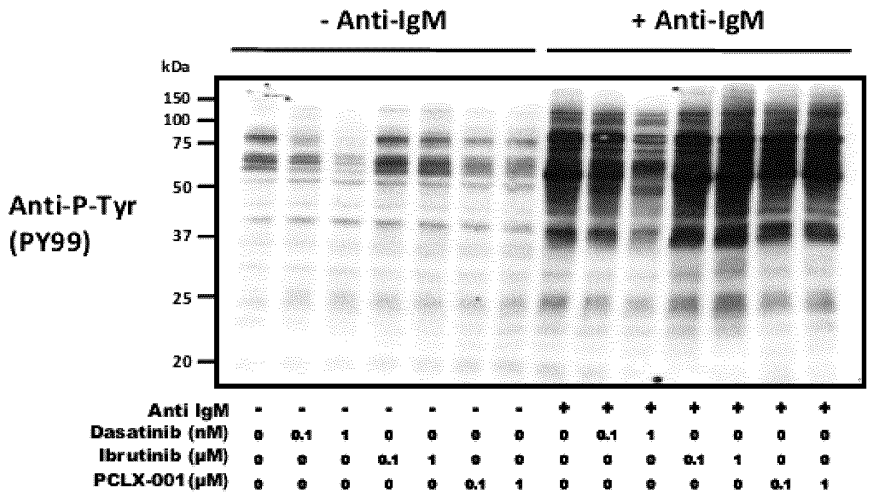


FIG. 15B

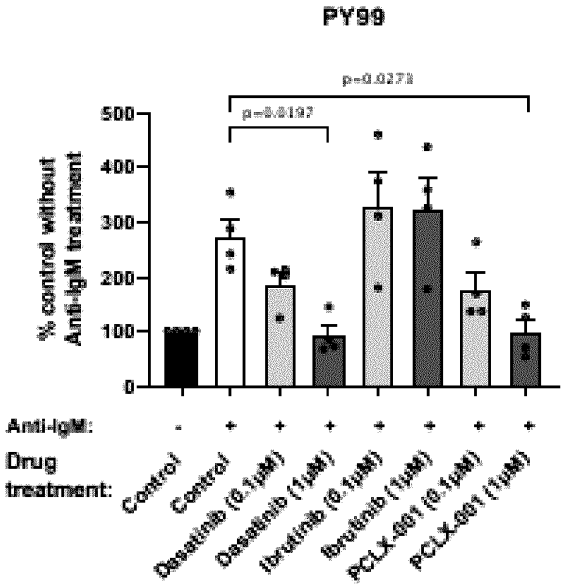


FIG. 16A

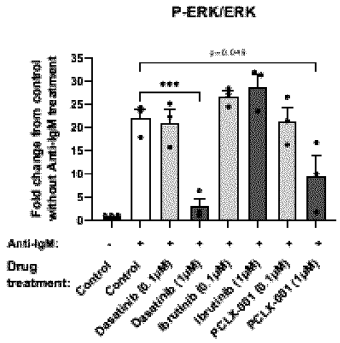


FIG. 16B

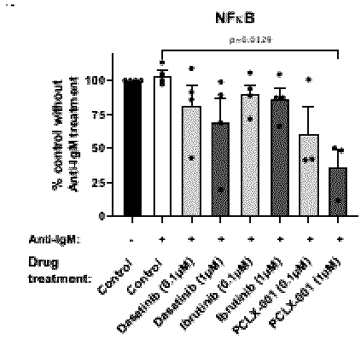


FIG. 16C

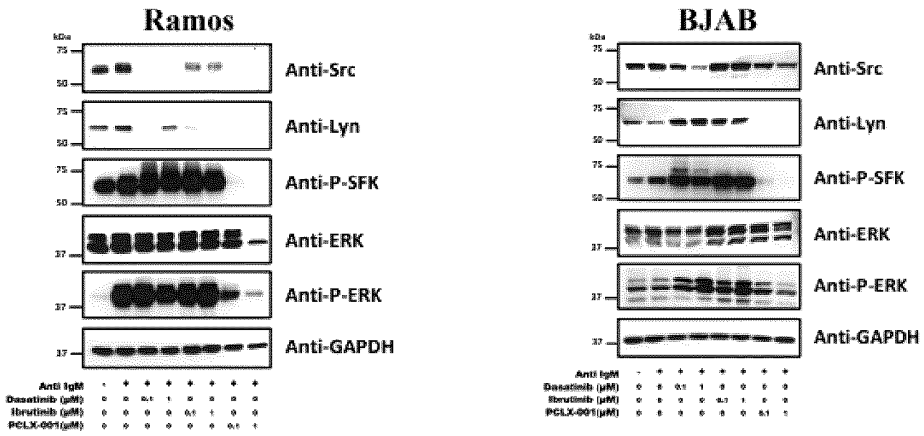

Ramos
BJAB
Anti-Src
Anti-Lyn
Anti-P-SFK
Anti-ERK
Anti-P-ERK
Anti-GAPDH

FIG. 17A

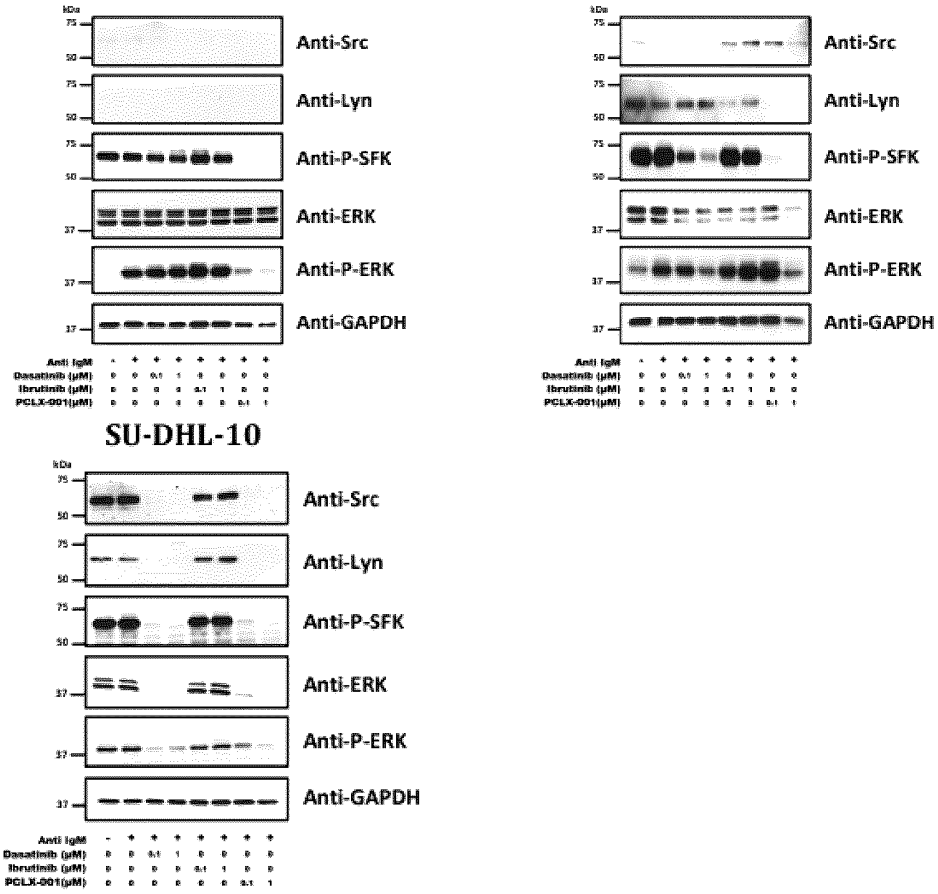

kDa
75
50
37
Anti-Src
Anti-Lyn
Anti-P-SFK
Anti-ERK
Anti-P-ERK
Anti-GAPDH
Anti IgM
Dasatinib (μM)
Ibrutinib (μM)
PCLX-001(μM)
SU-DHL-10

FIG. 17B

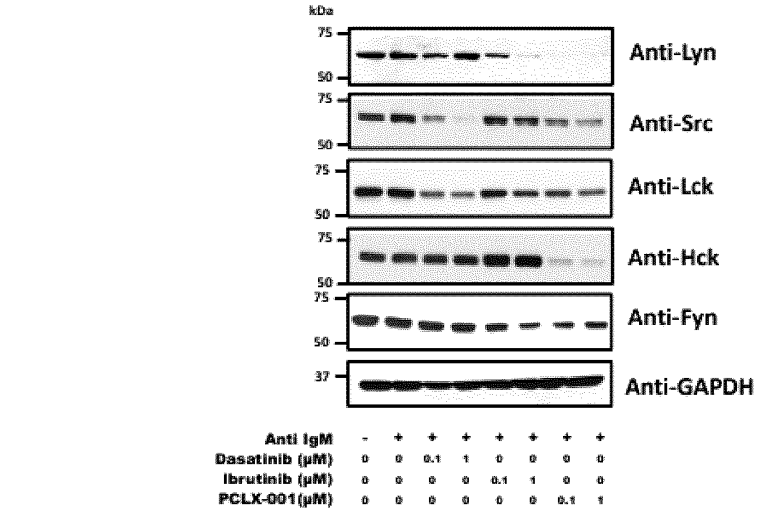


FIG. 18A

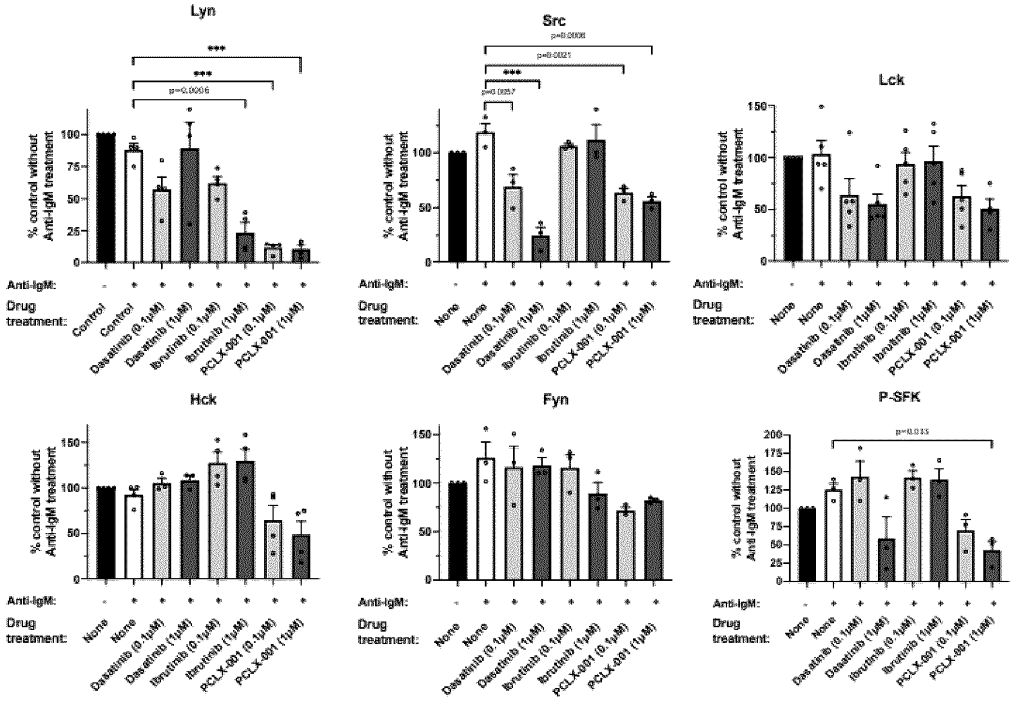


FIG. 18B

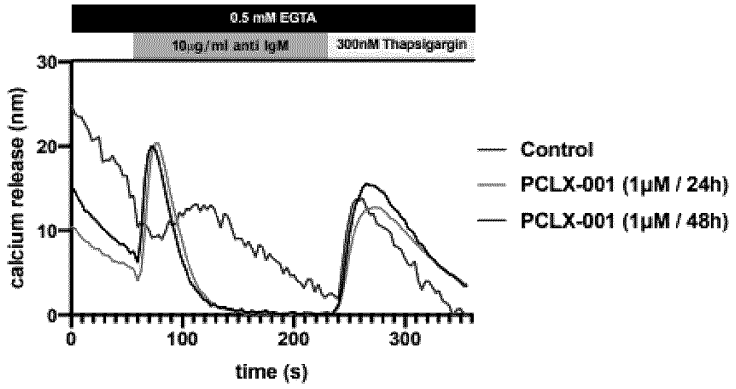


FIG. 19A

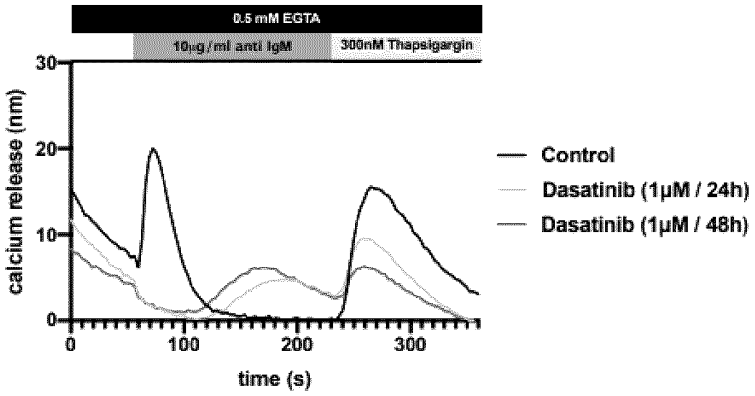


FIG. 19B

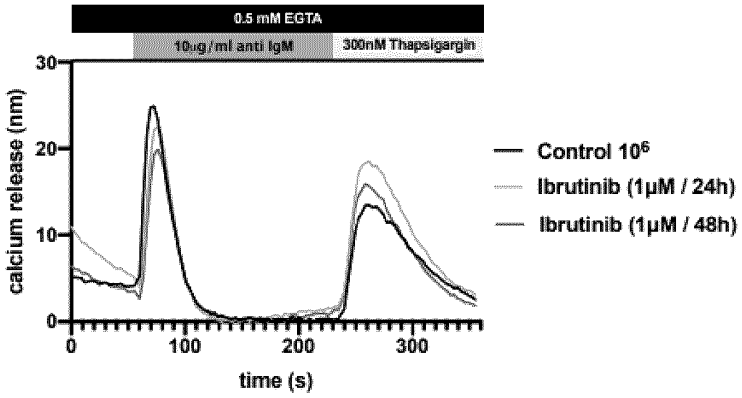


FIG. 19C

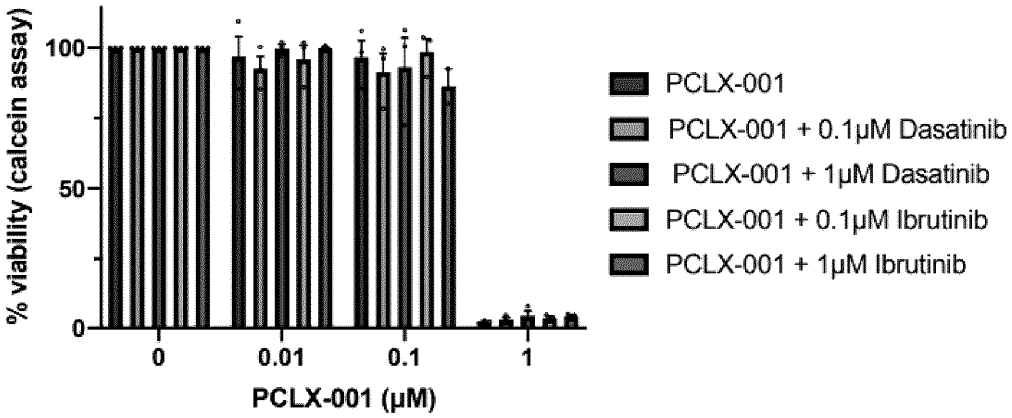


FIG. 20A

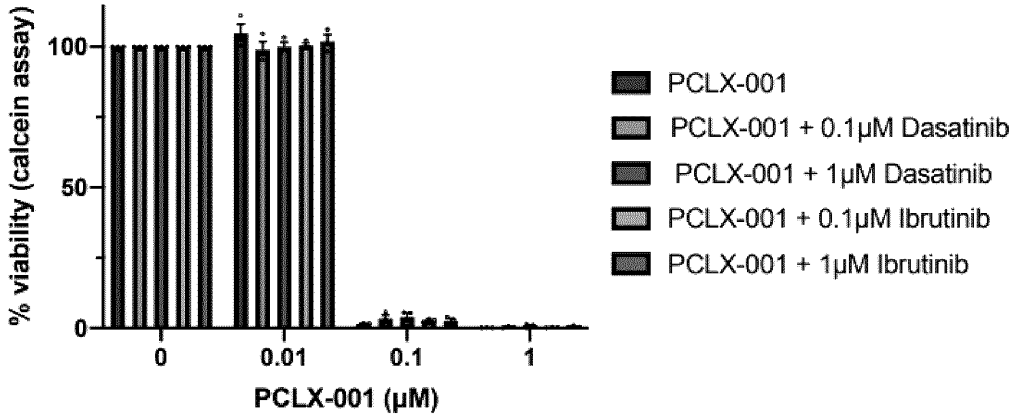


FIG. 20B

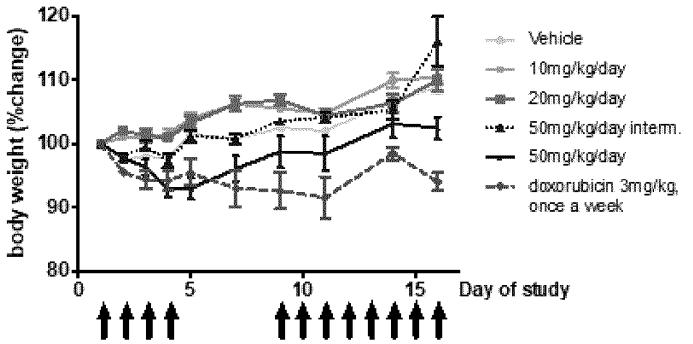


FIG. 21A

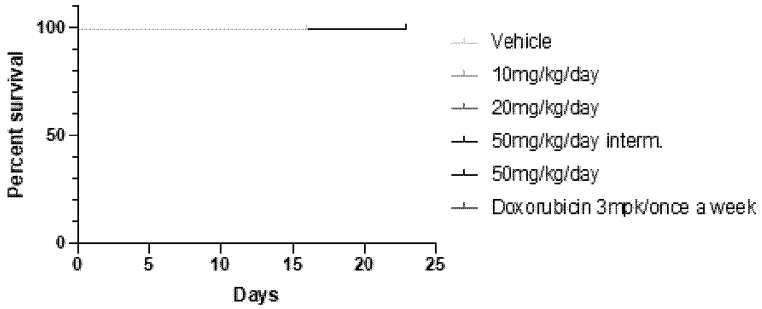


FIG. 21B

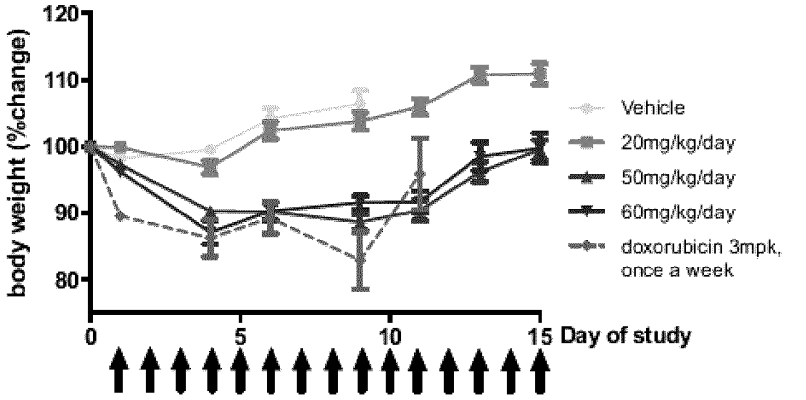


FIG. 21C

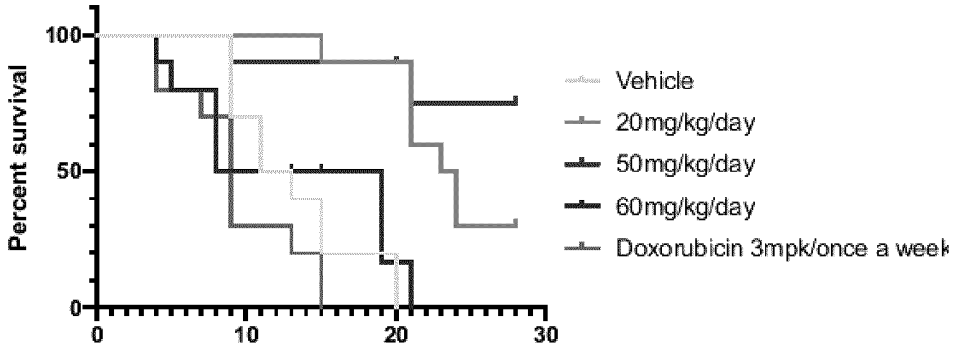


FIG. 21D

Drug	Dose	Median Survival (days)
Vehicle	---	12.0
PCLX-001	20mg/kg/day	23.5
	50mg/kg/day	Not Reached
	60mg/kg/day	13.5
Doxorubicin	3mg/kg/once a week	9.0

FIG. 21E

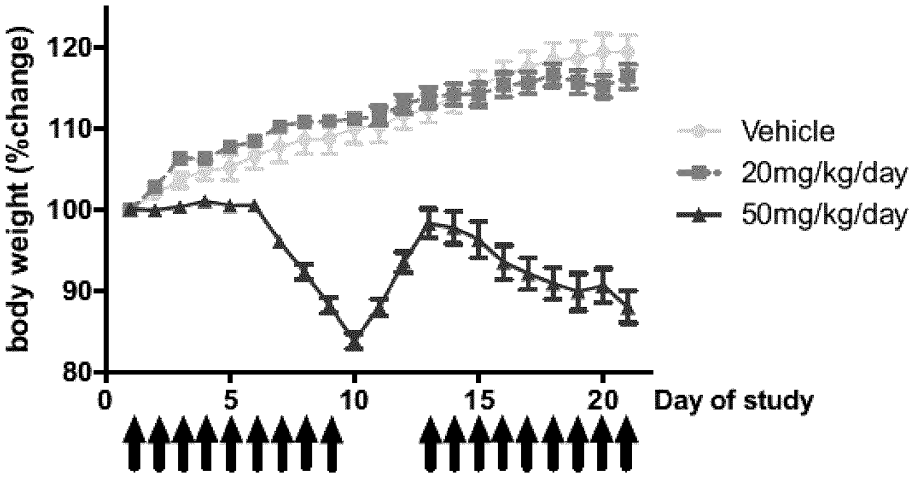


FIG. 21F

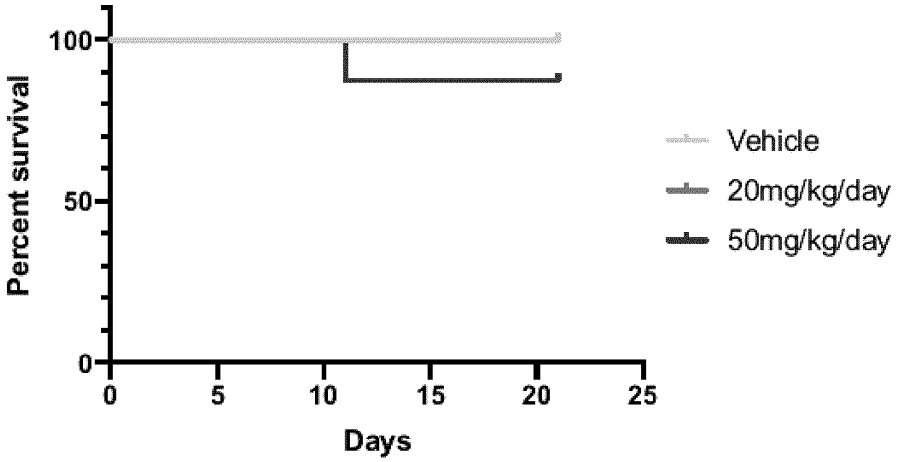


FIG. 21G

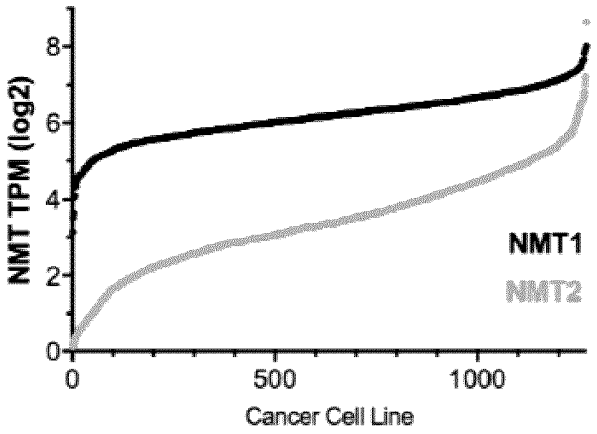


FIG. 22A

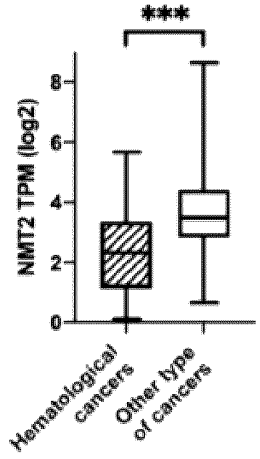


FIG. 22B

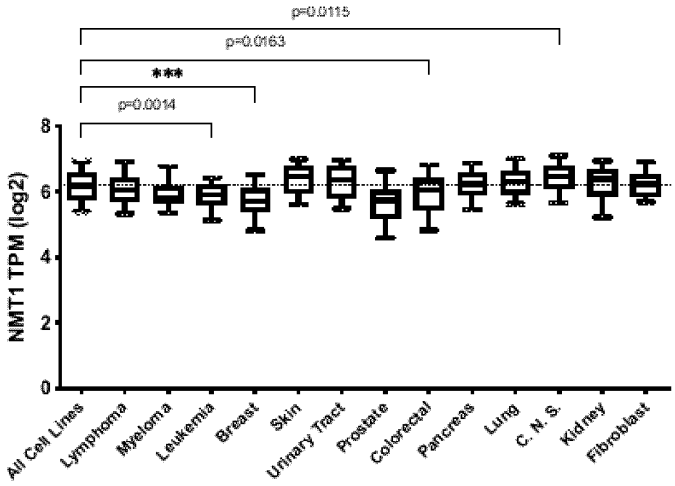


FIG. 22C

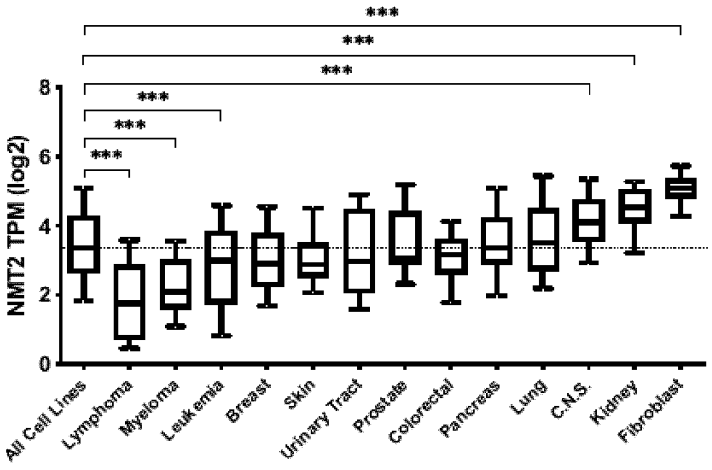


FIG. 22D

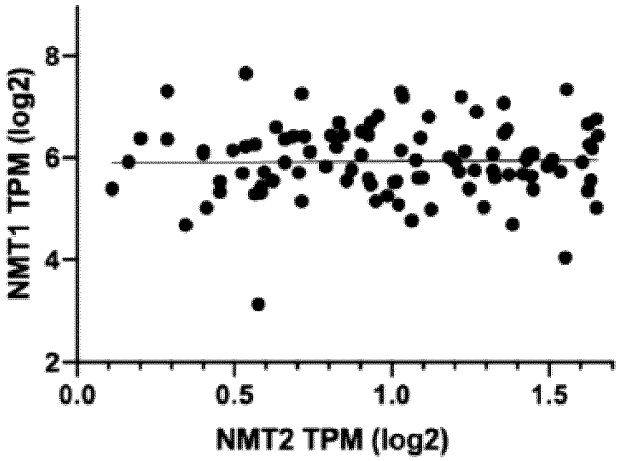


FIG. 22E

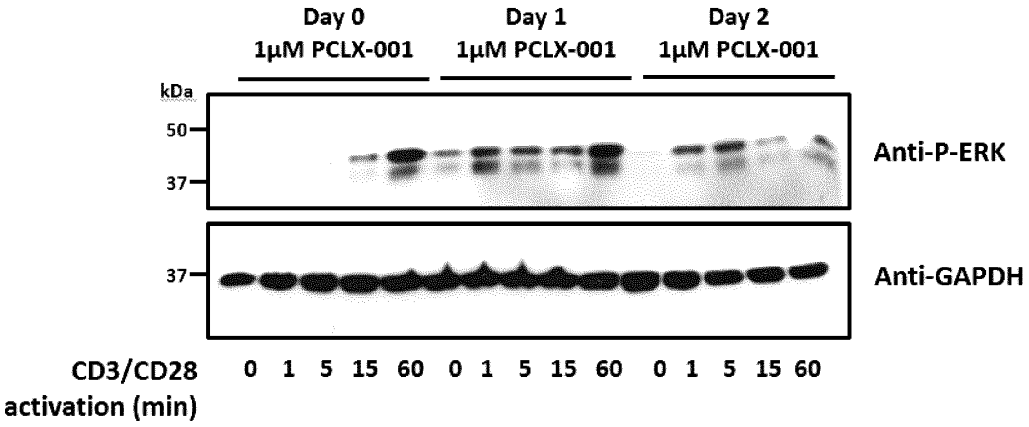


FIG. 23

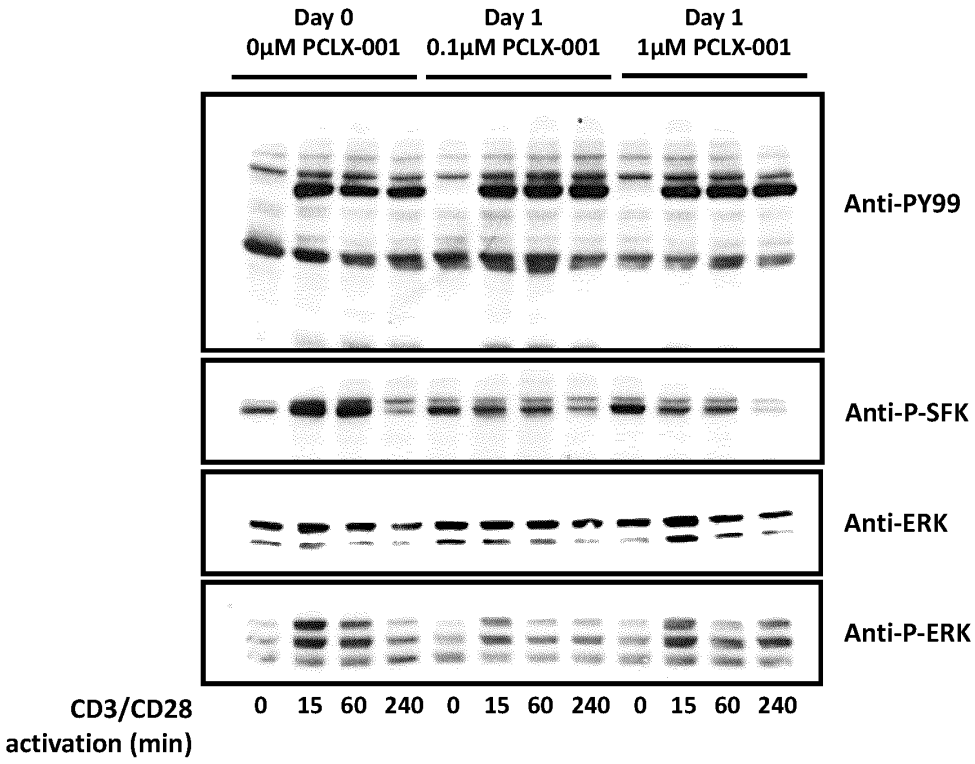

Day 0
0µM PCLX-001
Day 1
0.1µM PCLX-001
Day 1
1µM PCLX-001
Anti-PY99
Anti-P-SFK
Anti-ERK
Anti-P-ERK
CD3/CD28
activation (min)
0 15 60 240 0 15 60 240 0 15 60 240

FIG. 24

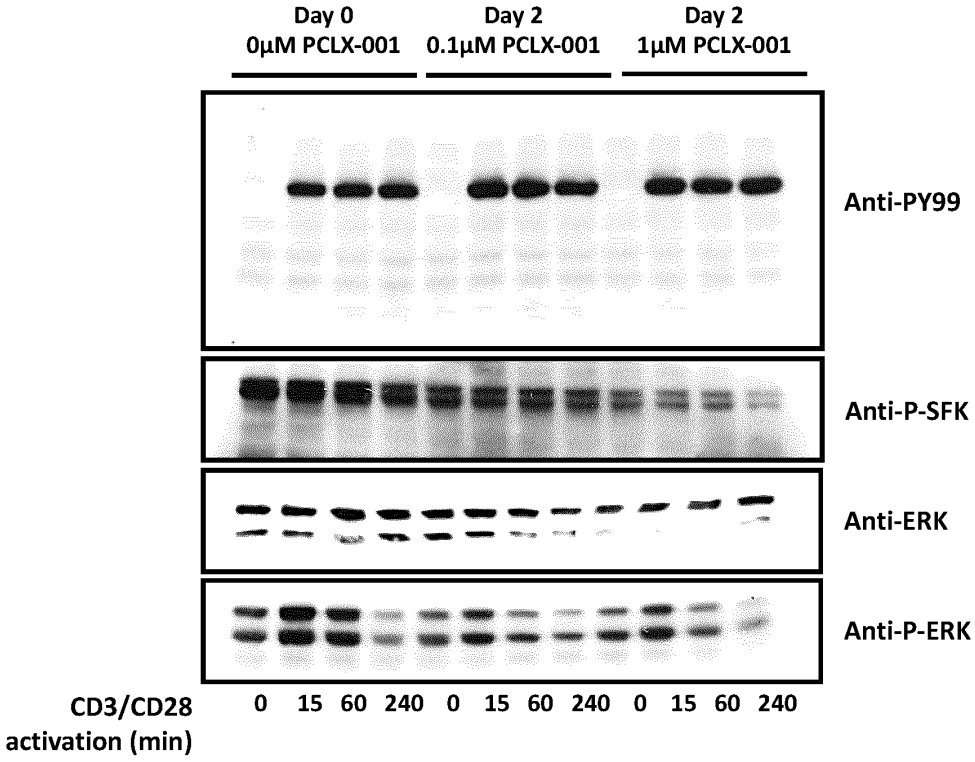

Day 0
0µM PCLX-001
Day 2
0.1µM PCLX-001
Day 2
1µM PCLX-001
Anti-PY99
Anti-P-SFK
Anti-ERK
Anti-P-ERK
CD3/CD28
activation (min)
0 15 60 240 0 15 60 240 0 15 60 240

FIG. 25

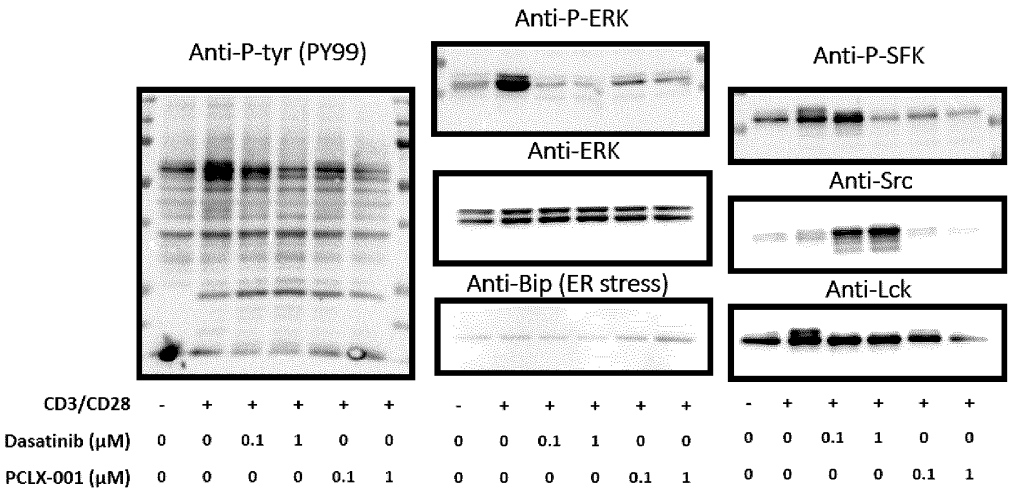


FIG. 26

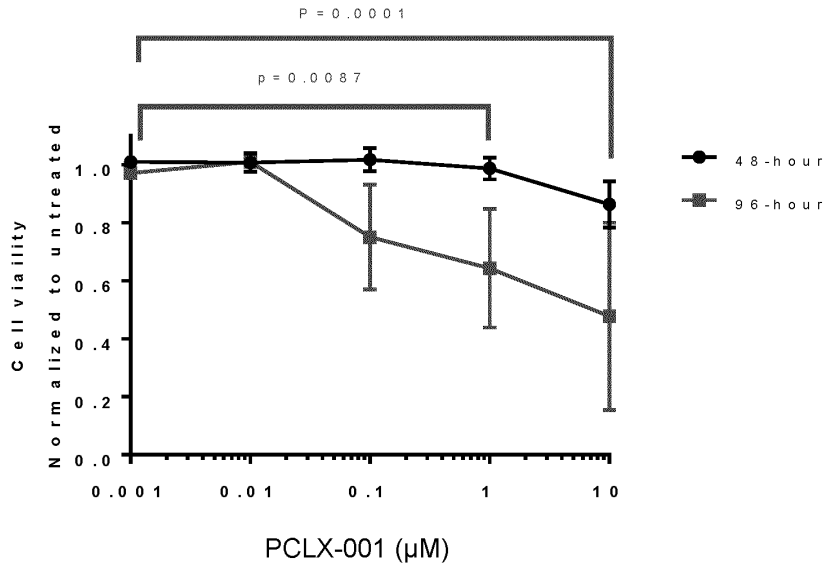


FIG 27A

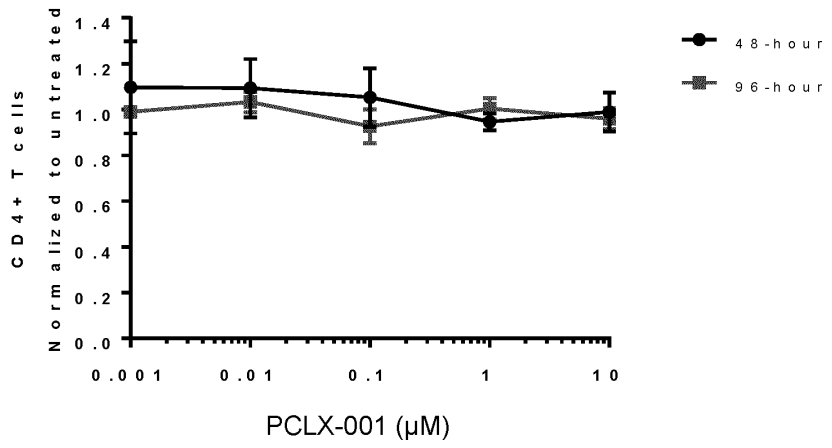


FIG 27B

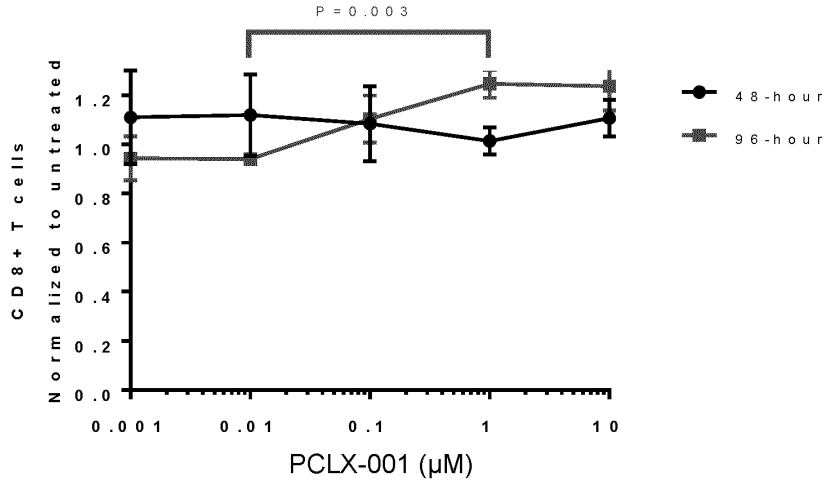


FIG 27C

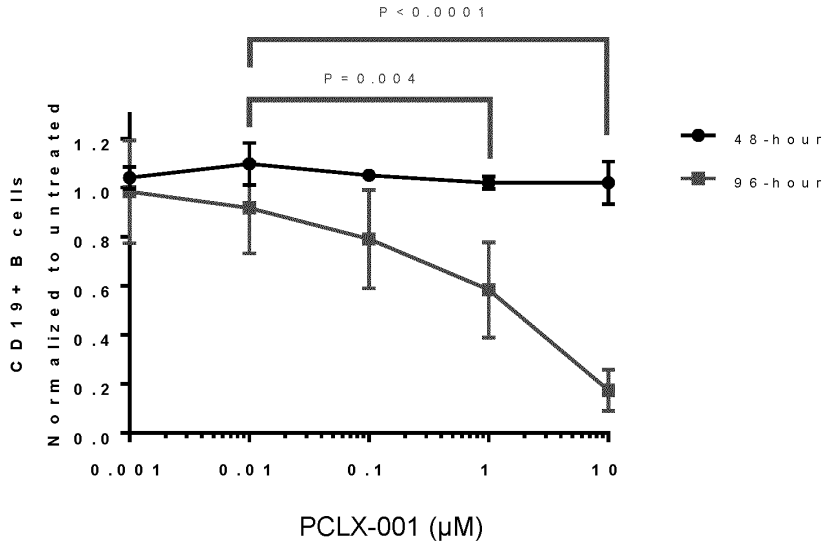


FIG 27D

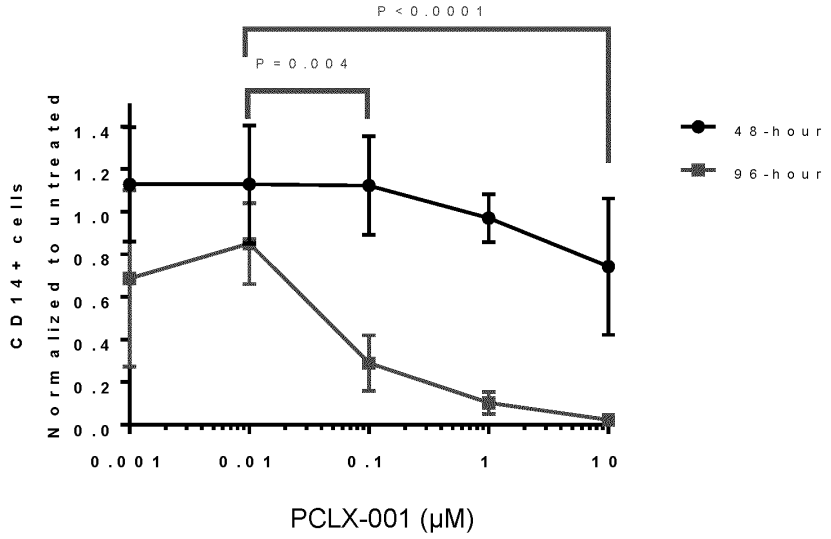


FIG 27E

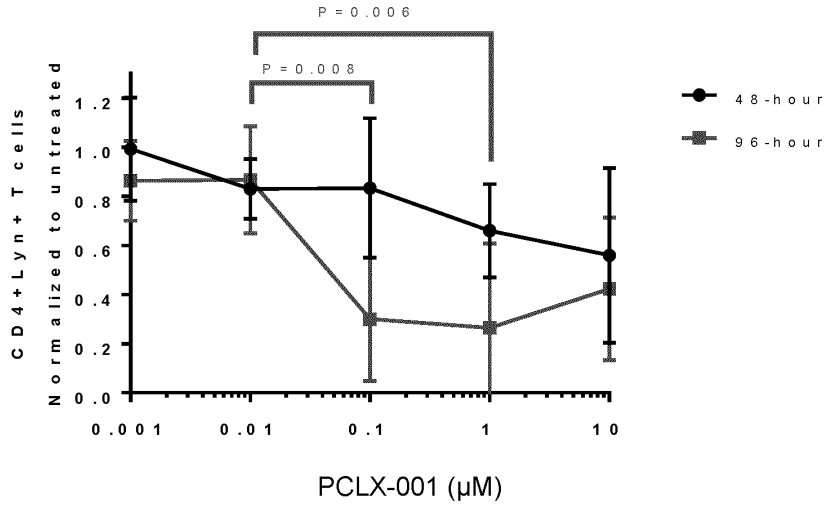


FIG 28A

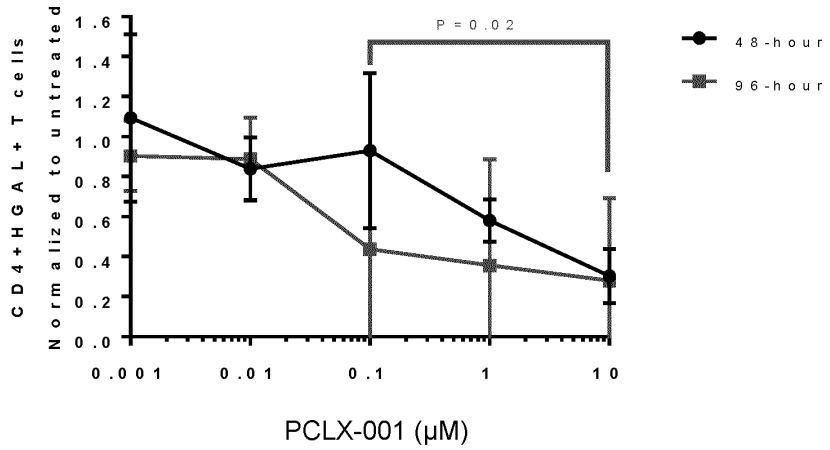


FIG 28B

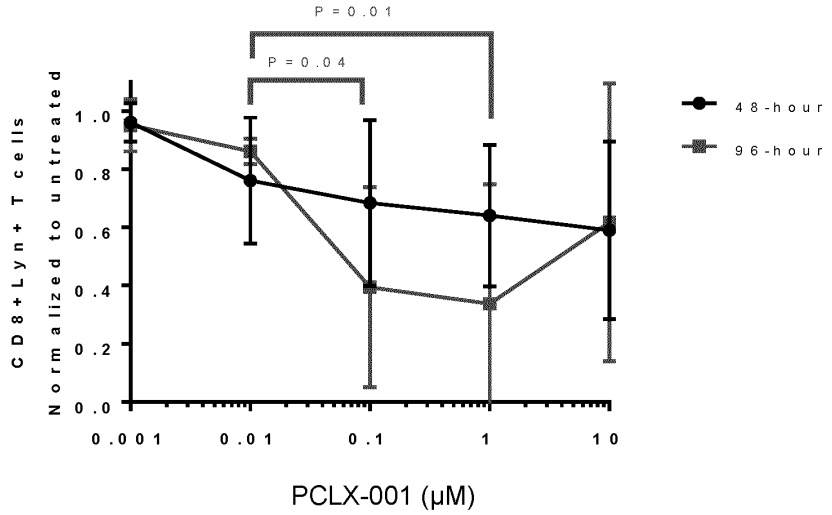


FIG 28C

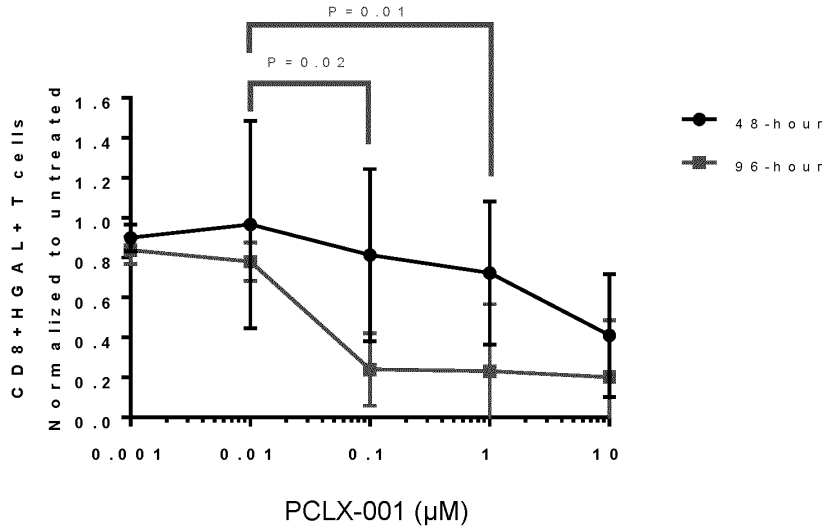


FIG 28D

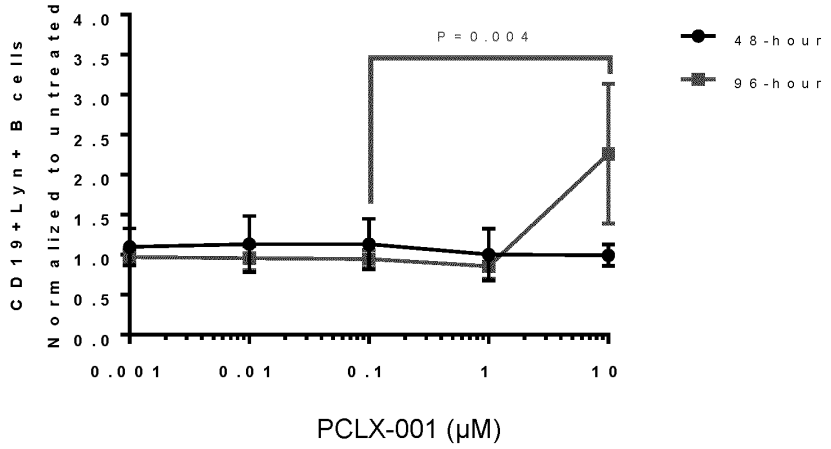


FIG 29A

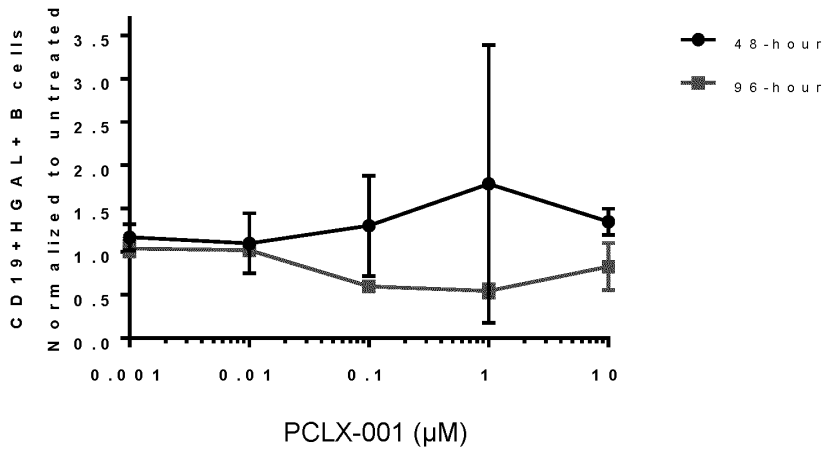


FIG 29B

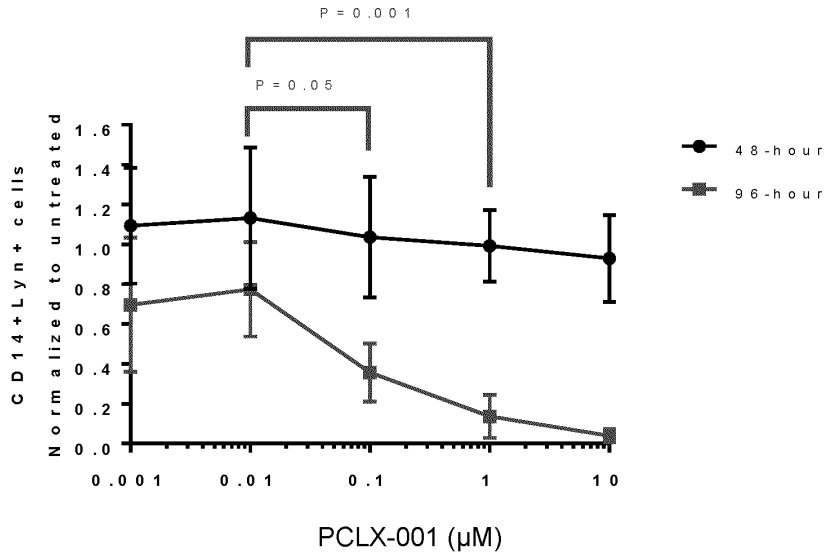


FIG 29C

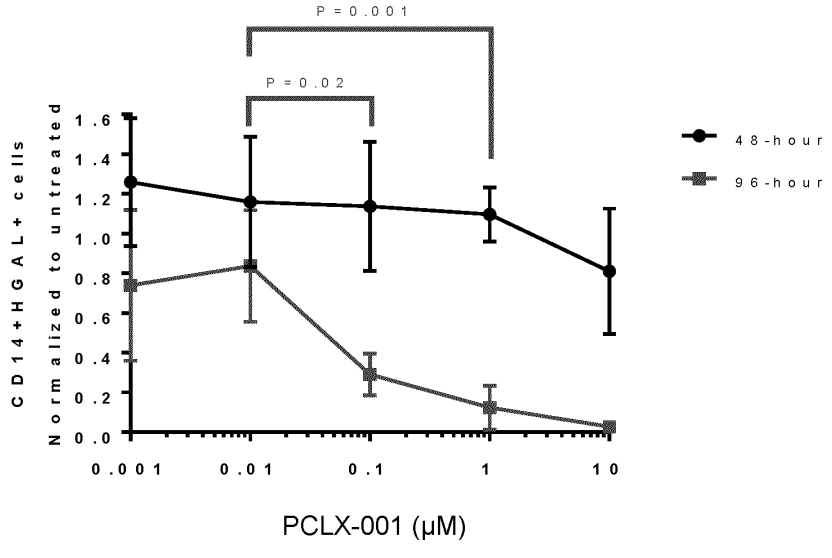


FIG 29D

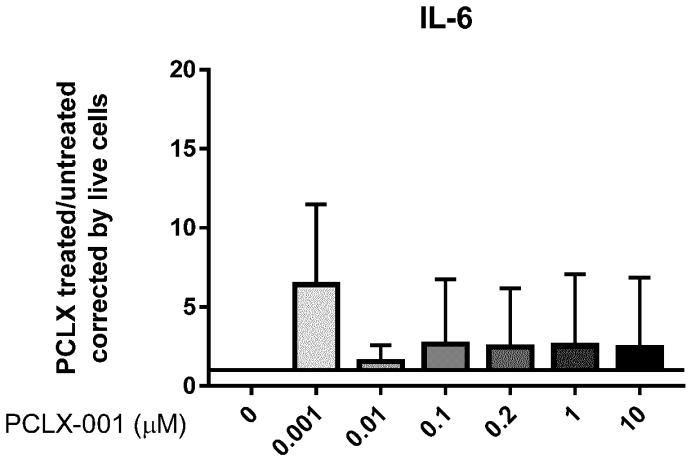


FIG 30A

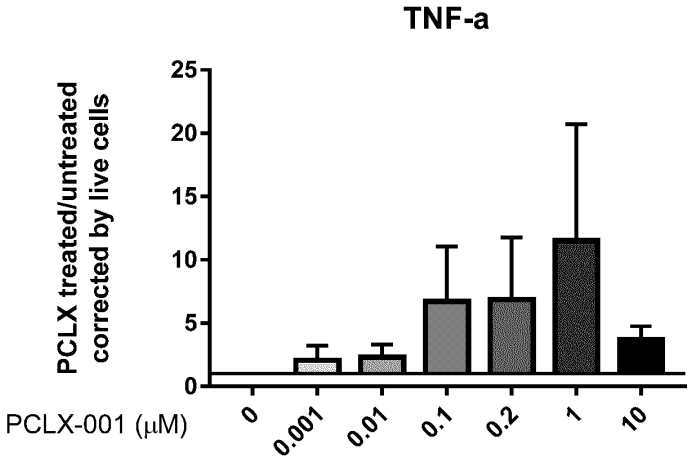


FIG 30B

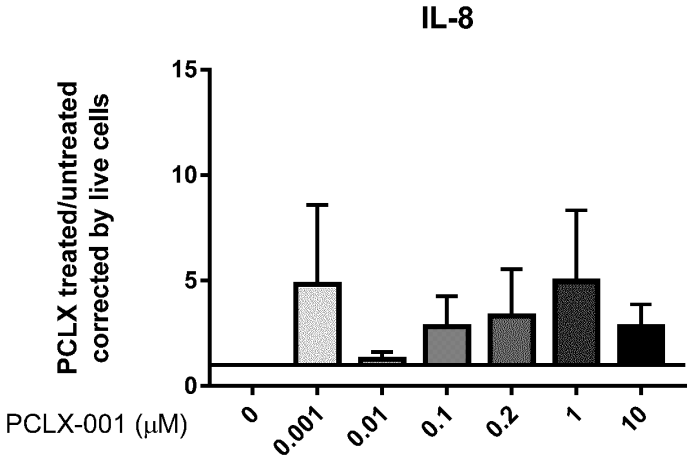


FIG 30C

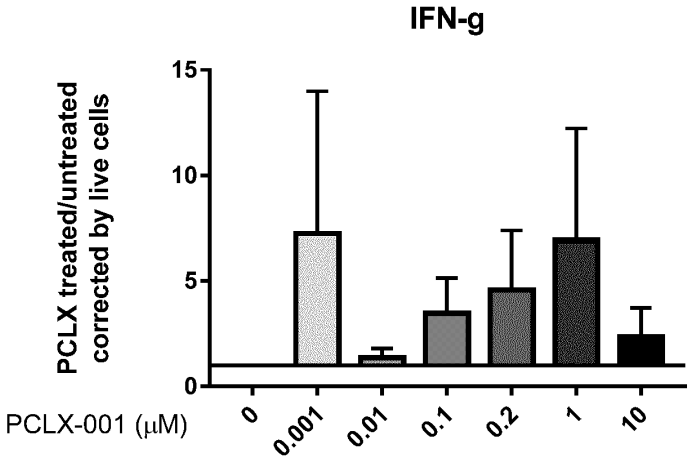


FIG 30D

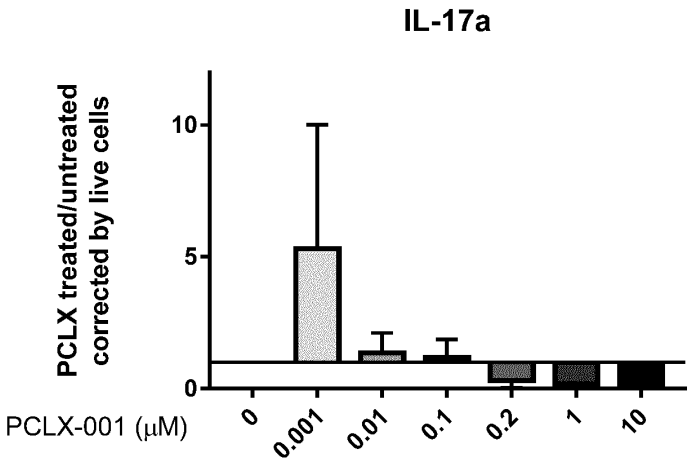


FIG 30E

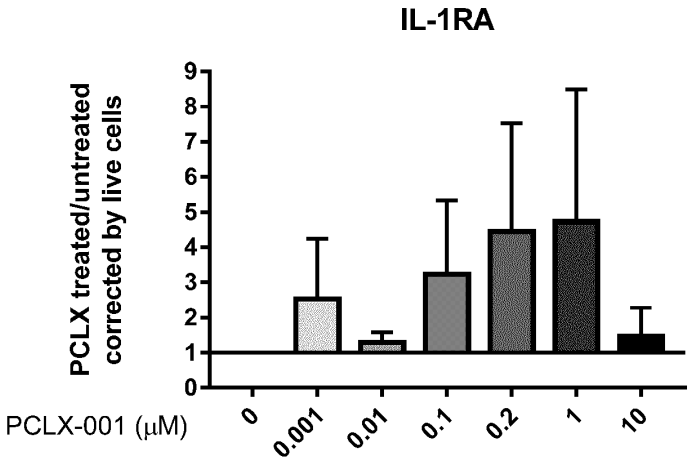


FIG 31A

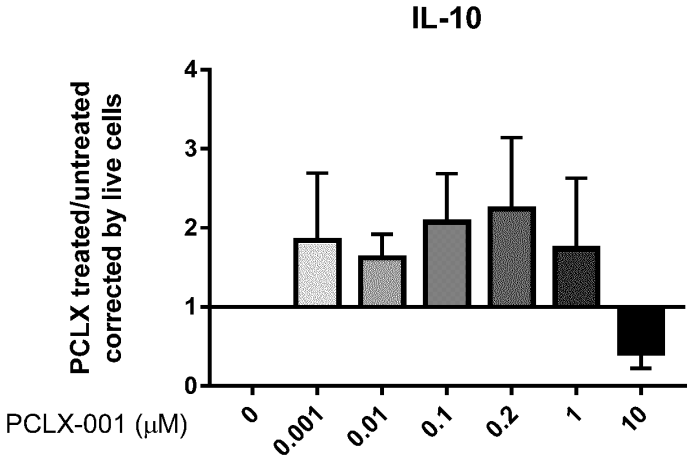


FIG 31B

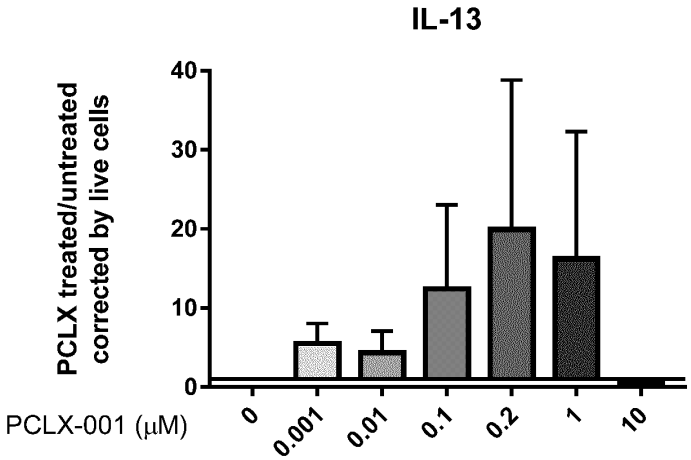


FIG 31C

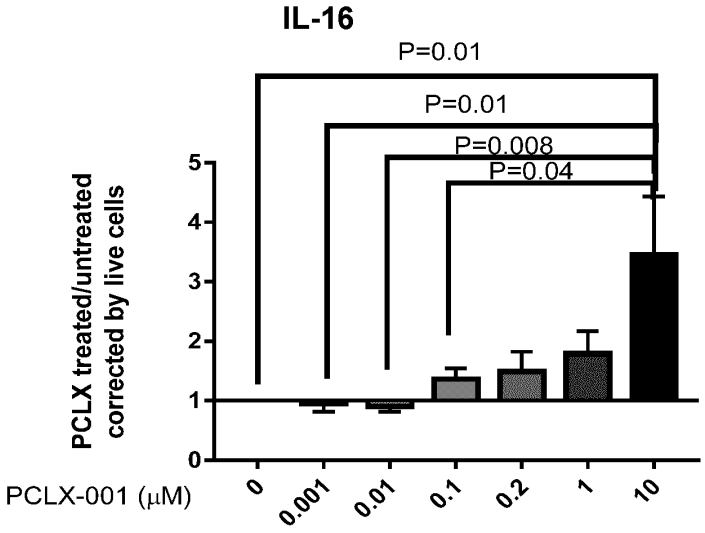


FIG 31D

FIG 32A

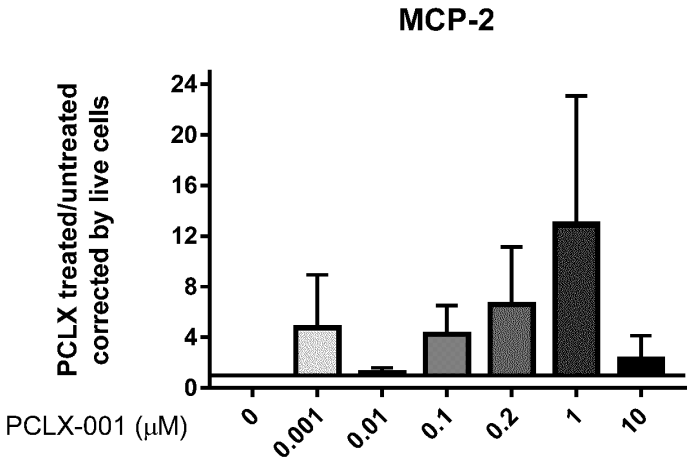


FIG 32B

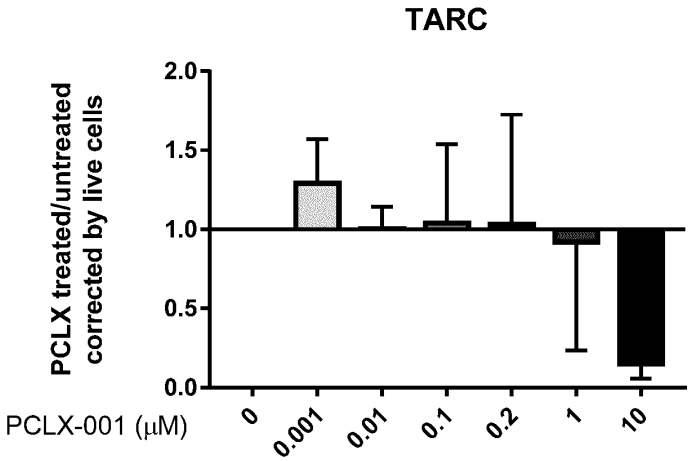


FIG 32C

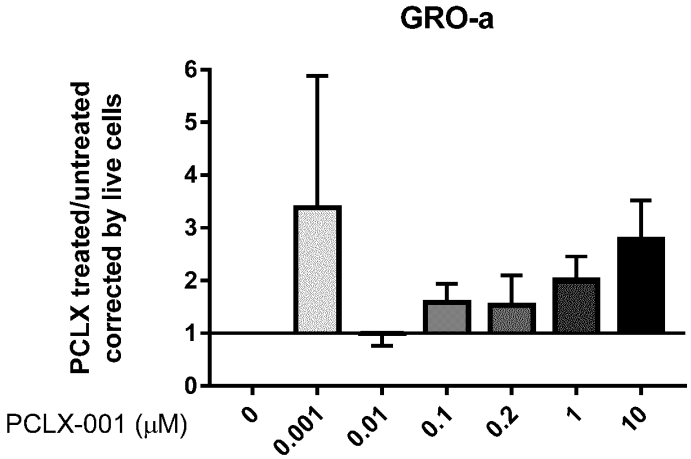


FIG 32D

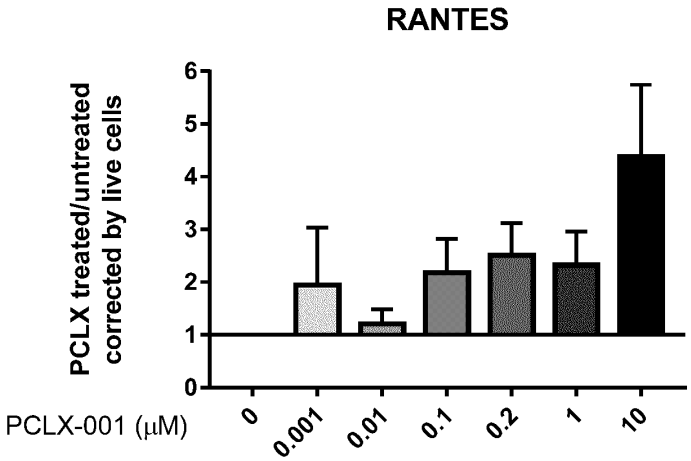


FIG 33A

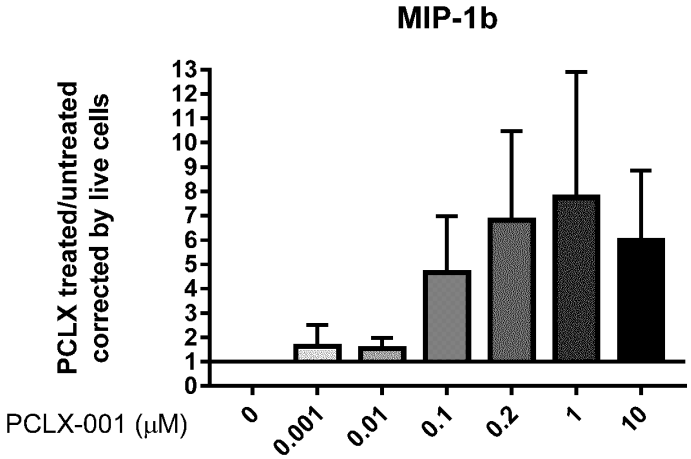


FIG 33B

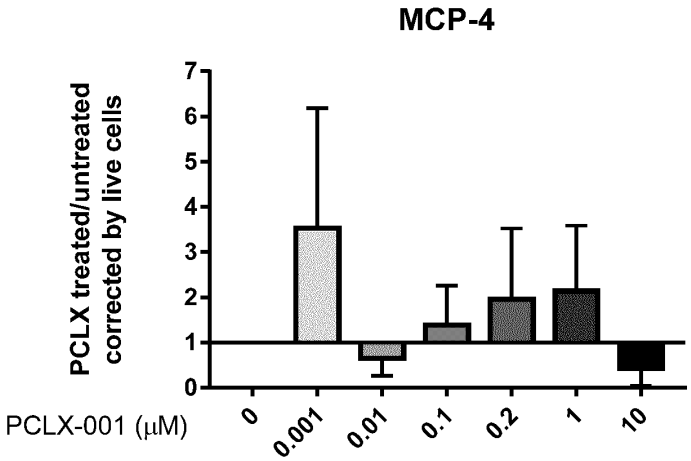


FIG 33C

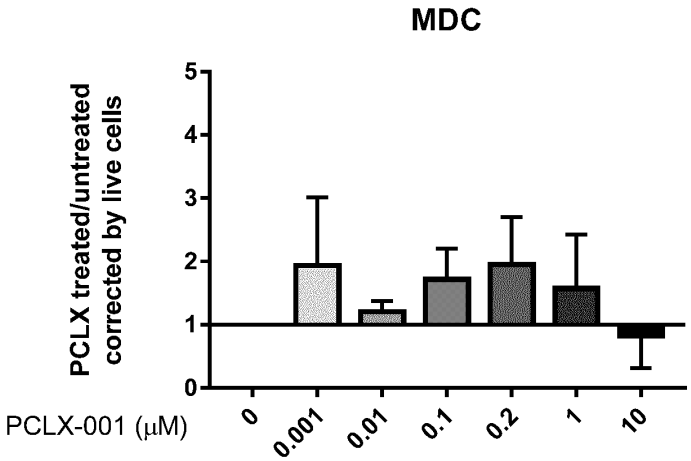


FIG 33D

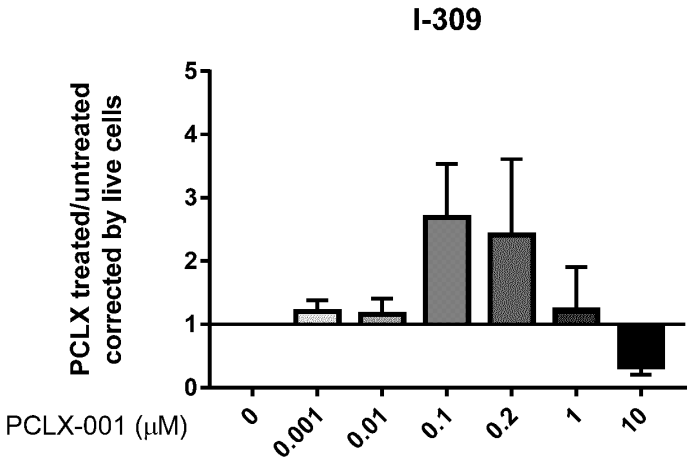


FIG 34A

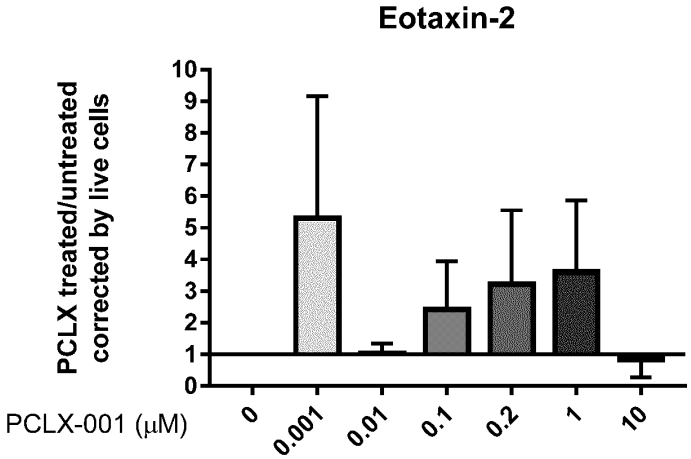


FIG 34B

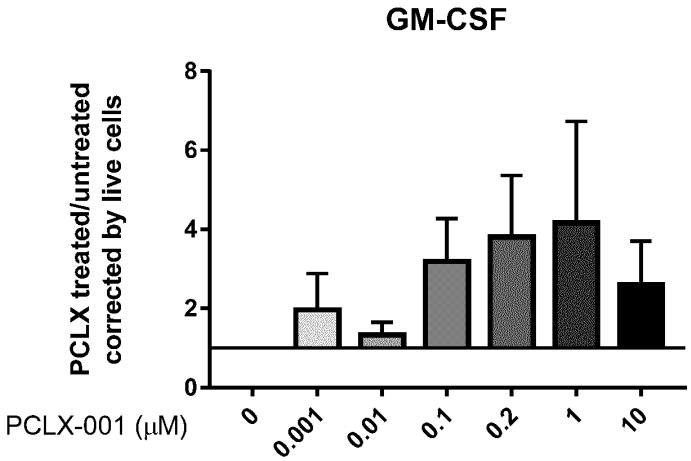


FIG 34C

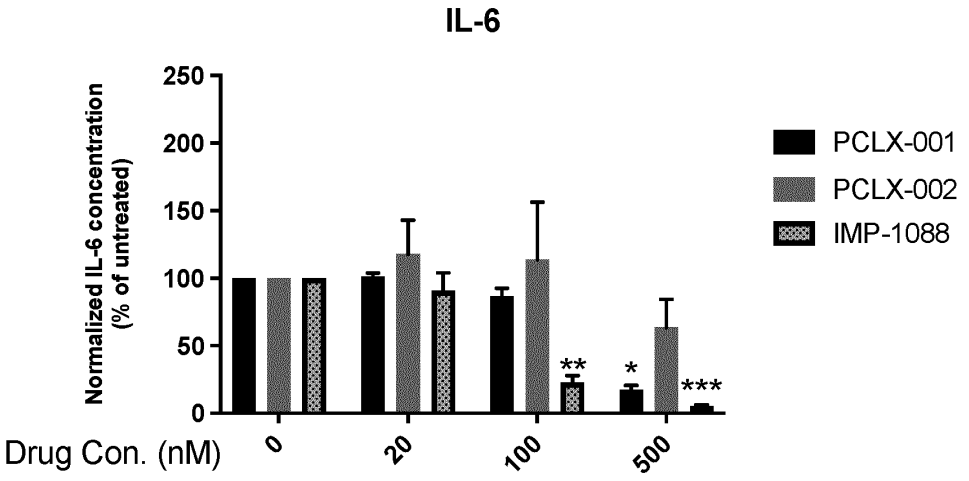


FIG 35A

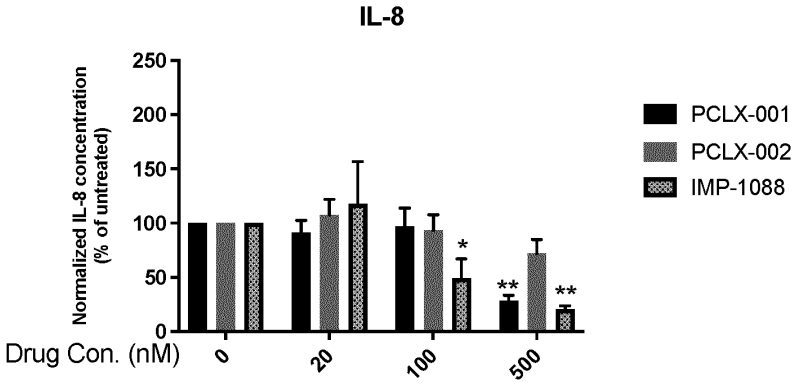


FIG 35B

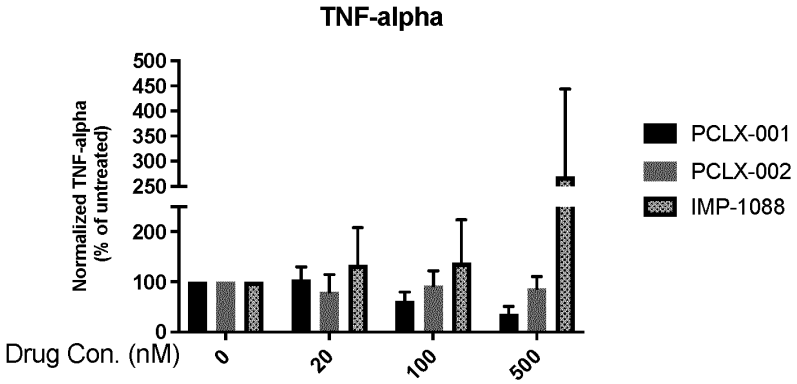


FIG 35C

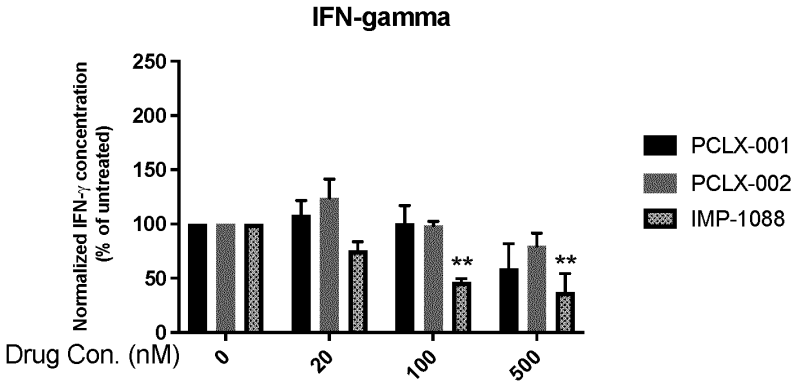


FIG35D

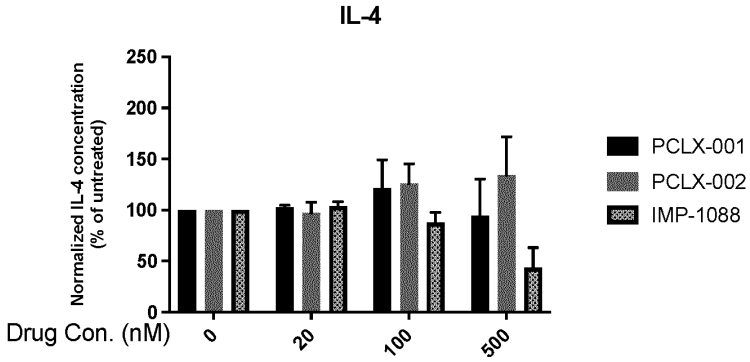


FIG 36A

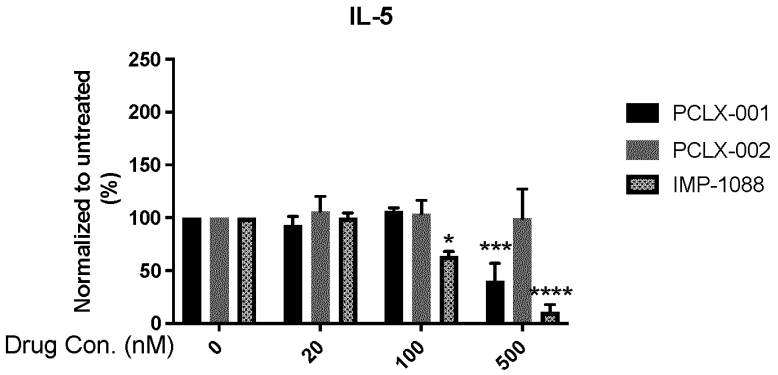


FIG 36B

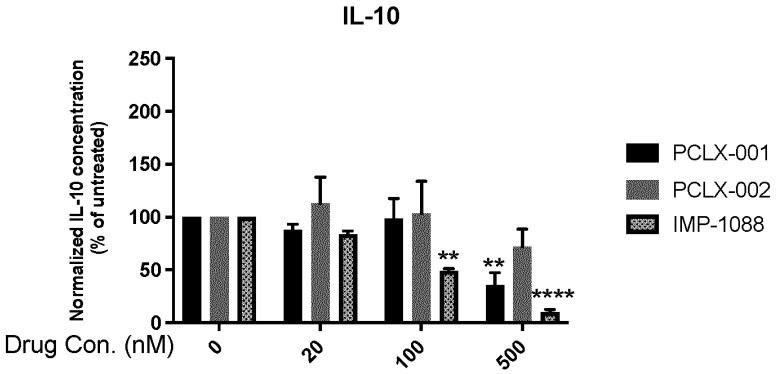


FIG 36C

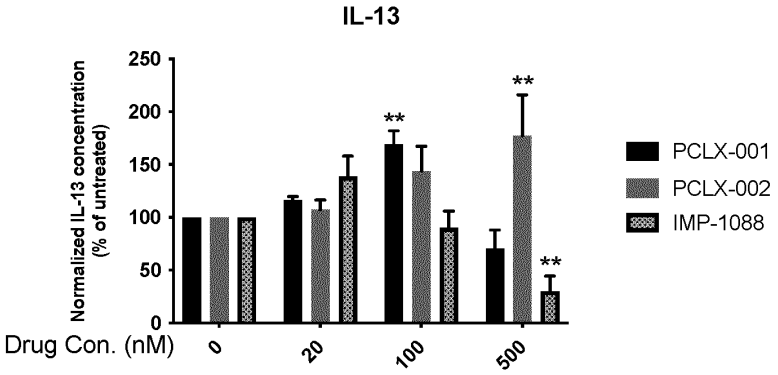


FIG 36D