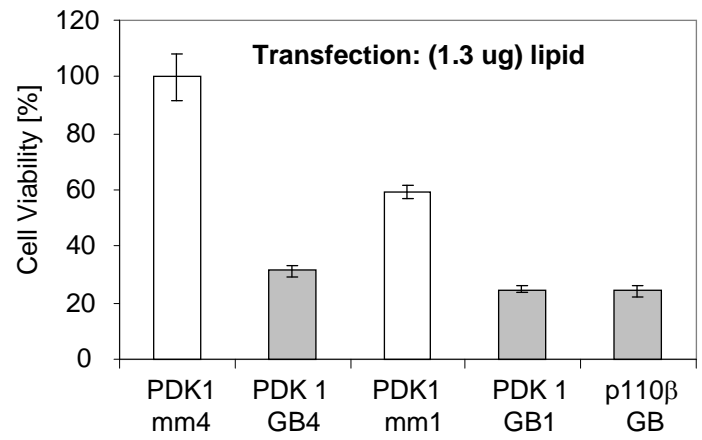
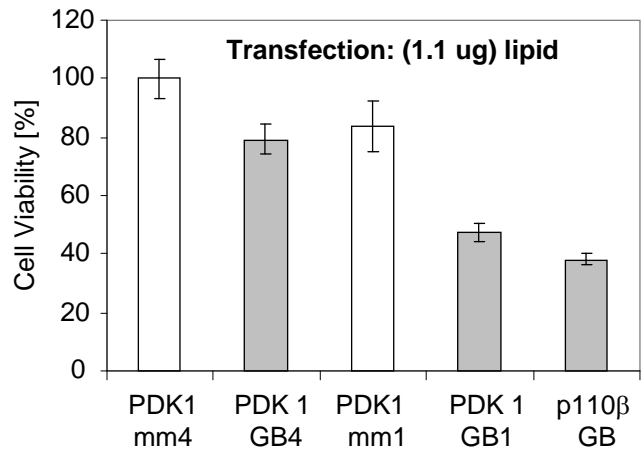
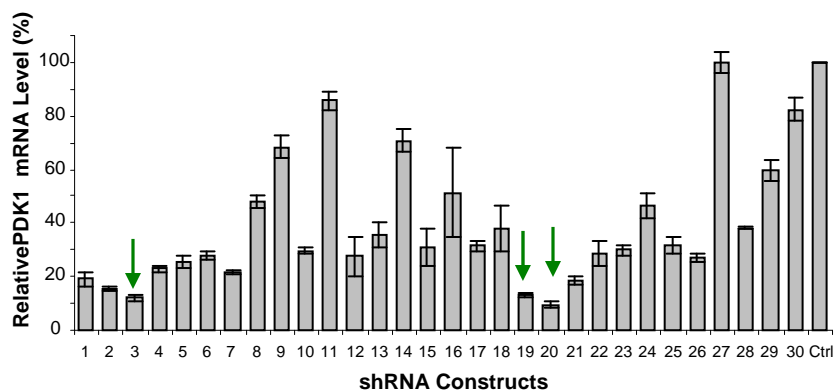


# Supplementary Figure S1

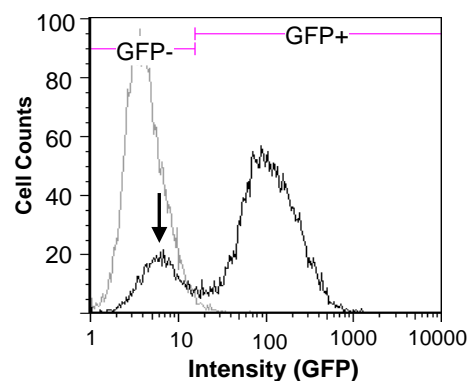


# Supplementary Figure S2

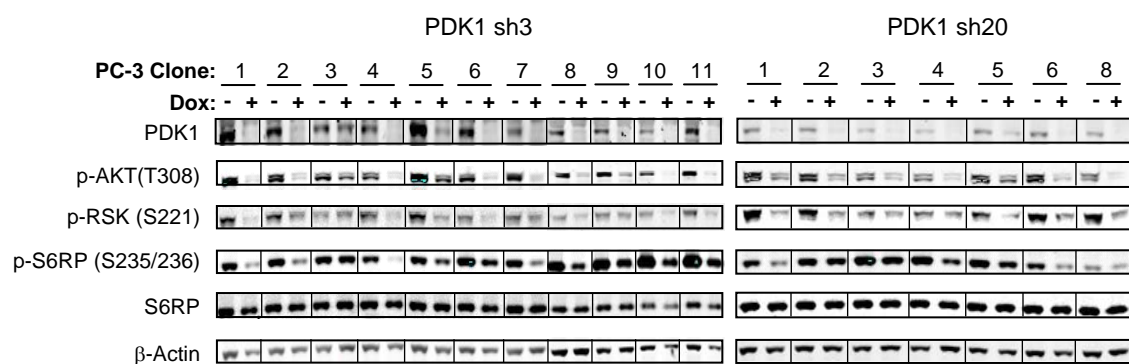
**a**



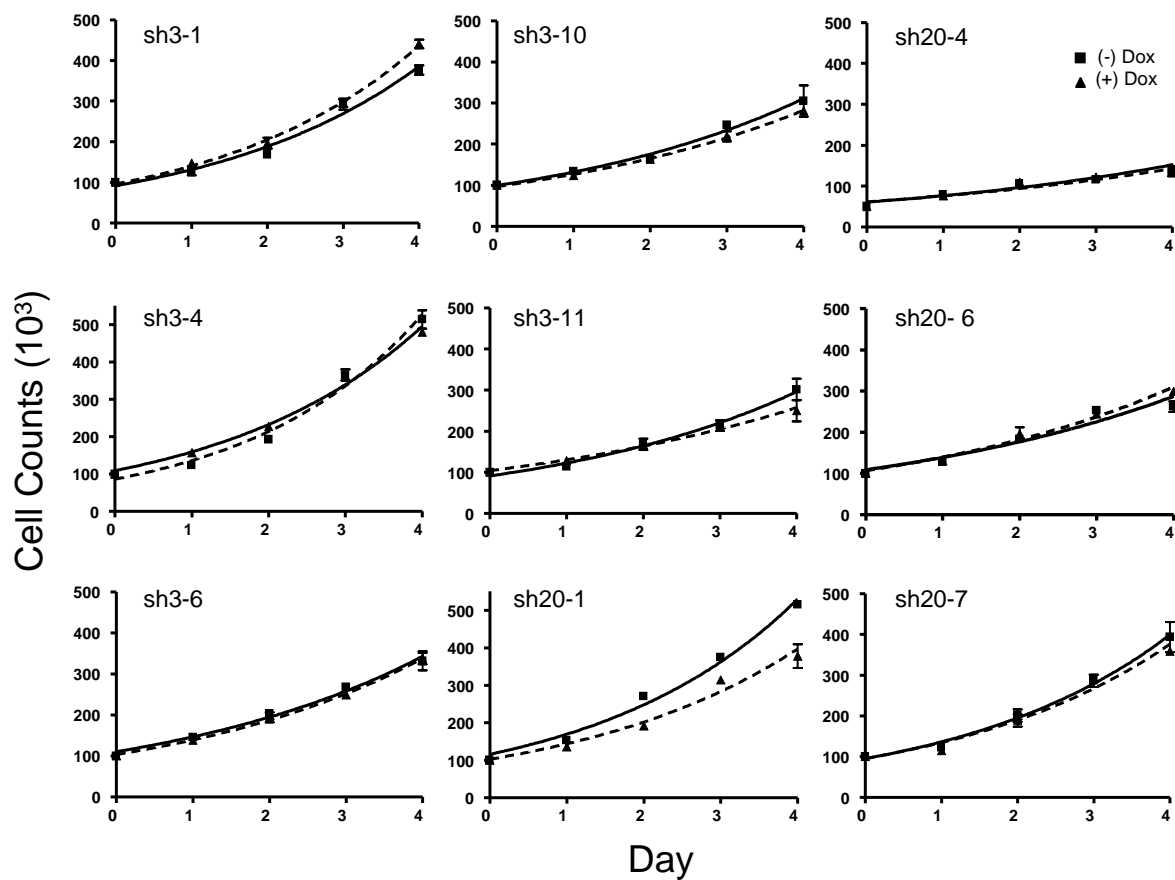
**b**



**c**



**d**



# Table S1. Kinase Selectivity Data for PDK1 Inhibitors

Cmpd 1 [10 μM]		Cmpd 2 [1 μM]		Cmpd 3 [1 μM]		Cmpd 4 [10 μM]		Cmpd 5 [1 μM]		Cmpd 6 [1 μM]		Cmpd 7 [10 μM]	
Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity
ABL(h)	86	ABL(h)	71	ABL(h)	73	ABL(h)	73	ABL(h)	112	ABL(h)	112	ABL(h)	112
ACK(h)	66	Abi (H396P)(h)	49	Abi(T315I)(h)	113	Abi(T315I)(h)	62	ABL(m)	98	Abi (H396P)(h)	114	Abi (H396P)(h)	114
AKT1(h)	39	Abi(M35T1)(h)	50	ALK(h)	100	ALK(h)	42	ABL(T315I)(h)	86	Abi(M35T1)(h)	110	Abi(M35T1)(h)	110
ALK(h)	26	Abi(Q252H)(h)	54	ALK4(h)	99	ALK4(h)	18	ABL2(h)	111	Abi(Q252H)(h)	69	Abi(Q252H)(h)	69
AMPK(α)	12	Abi(T315I)(h)	88	Arg(h)	97	Arg(h)	78	ABL2(m)	110	Abi(T315I)(h)	91	Abi(T315I)(h)	91
AURKC(h)	4	Abi(Y235F)(h)	60	ARR5(h)	8	ARR5(h)	66	AKT1(h)	102	Abi(Y235F)(h)	110	Abi(Y235F)(h)	110
BRAF(h)	114	ASK1(h)	32	ASK1(h)	65	ASK1(h)	77	AKT2(h)	94	ASK1(h)	94	ASK1(h)	94
BRK2(h)	1	ALK(h)	77	Aurora-A(h)	0	Aurora-A(h)	8	AKT3(h)	90	ALK(h)	116	ALK(h)	116
BT(h)	83	ALK4(h)	93	Axl(h)	93	Axl(h)	3	ALK(h)	116	ALK4(h)	115	ALK4(h)	115
CDC7(h)	70	Arg(h)	104	Bmx(h)	94	Bmx(h)	25	ALK4(h)	138	Arg(h)	112	Arg(h)	112
CDK2/CNA3(h)	53	ARR5(h)	11	BRK(h)	97	BRK(h)	81	AMPK(α)	104	ARR5(h)	112	ARR5(h)	112
CDK4(h)	21	ASK1(h)	7	BRK1(h)	76	BRK1(h)	36	ARR5(h)	4	ASK1(h)	106	ASK1(h)	106
CHK1(h)	10	Aurora-A(h)	104	BRK2(h)	81	BRK2(h)	57	AURK4(h)	104	Aurora-A(h)	99	Aurora-A(h)	99
CSK(h)	101	Axl(h)	18	BT(h)	76	BT(h)	75	Axl(h)	96	Axl(h)	107	Axl(h)	107
CSNK1(α)	59	Bmx(h)	89	CaMKI(h)	97	CaMKI(h)	9	BLK(m)	92	Bmx(h)	107	Bmx(h)	107
CSNK2(α)	43	BRK(h)	105	CaMKIβ(h)	20	CaMKIβ(h)	6	BMX(h)	94	BRK(h)	94	BRK(h)	94
CSNK2A1(h)	71	BrSk1(h)	29	CaMKII(h)	97	CaMKII(h)	58	BRSK2(h)	18	BrSk1(h)	139	BrSk1(h)	139
DNA-PK(h)	87	BRK2(h)	15	CaMKIβ(h)	3	CaMKIβ(h)	11	BT(h)	95	BRK2(h)	116	BRK2(h)	116
DYRK1A(h)	64	CaMKI(h)	79	CaMKII(h)	102	CaMKII(h)	69	CaMK(h)	45	CaMKI(h)	109	CaMKI(h)	109
EGFR(h)	75	BT(h)	100	CaMKIβ(h)	86	CaMKIβ(h)	47	CaMK4(h)	61	BT(h)	111	BT(h)	111
EPHA2(h)	96	CaMKI(h)	63	CDK1/cyclinB(h)	99	CDK1/cyclinB(h)	90	CaMKI(α)	79	CaMKI(h)	107	CaMKI(h)	107
EPHA4(h)	101	CaMKII(h)	78	CDK2/cyclinA(h)	99	CDK2/cyclinA(h)	118	CDCA2BP(h)	105	CaMKII(h)	106	CaMKII(h)	106
ERBB2(h)	130	CaMKII(h)	13	CDK2/cyclinE(h)	107	CDK2/cyclinE(h)	99	GDK1(h)	183	CDK2/cyclinA(h)	96	CDK2/cyclinA(h)	96
ERK2/MAPK1(α)	11	CaMKIβ(h)	25	CDK3/cyclinE(h)	89	CDK3/cyclinE(h)	84	CDK2(h)	107	CaMKIβ(h)	105	CaMKIβ(h)	105
FGFR1(h)	30	CDK5/p25(h)	22	CDK5/p25(h)	46	CDK5/p25(h)	82	CDK2(h)	102	CDK5/p25(h)	97	CDK5/p25(h)	97
FGFR3(h)	32	CaMKIβ(h)	55	CDK5/p35(h)	47	CDK5/p35(h)	98	CDK3(h)	96	CaMKIβ(h)	92	CaMKIβ(h)	92
FLT3(h)	25	CDK1/cyclinB(h)	100	CDK6/cyclinD3(h)	86	CDK6/cyclinD3(h)	103	CDK5(h)	114	CDK1/cyclinB(h)	96	CDK1/cyclinB(h)	96
GSK3β(h)	83	CDK1/cyclinA(h)	104	CDK7/cyclinH/MAT1(h)	75	CDK7/cyclinH/MAT1(h)	73	CDK5(h)	103	CDK1/cyclinA(h)	103	CDK1/cyclinA(h)	103
IGF1R(h)	61	CDK2/cyclinE(h)	116	CDK9/cyclin T1(h)	70	CDK9/cyclin T1(h)	126	CDK6(h)	106	CDK2/cyclinE(h)	111	CDK2/cyclinE(h)	111
IKK_BETA(h)	15	CDK3/cyclinE(h)	106	CHK1(h)	54	CHK1(h)	75	CDK7(h)	55	CDK3/cyclinE(h)	104	CDK3/cyclinE(h)	104
JNK1(h)	28	CHK2(h)	122	CHK2(h)	60	CHK2(h)	5	CHK2(h)	5	CHK1(h)	113	CHK1(h)	113
JNK1A1(h)	10	CHK2(h)	104	CHK2(R157T)(h)	71	CHK2(R157T)(h)	6	CHK1(h)	6	CHK2(h)	113	CHK2(h)	113
KDR(h)	92	CDK6/cyclinD3(h)	102	CHK2(R145W)(h)	101	CHK2(R145W)(h)	1	CK2(h)	103	CDK6/cyclinD3(h)	111	CDK6/cyclinD3(h)	111
KIT(h)	40	CDK7/cyclinH/MAT1(h)	102	CK1γ1(h)	112	CK1γ1(h)	51	CSF1R(h)	55	CK1γ1(h)	97	CK1γ1(h)	97
LCK(h)	26	CDK9/cyclin T1(h)	96	CK1γ2(h)	89	CK1γ2(h)	39	CSK(h)	110	CDK9/cyclin T1(h)	102	CDK9/cyclin T1(h)	102
MAP3K14(h)	92	CHK1(h)	46	CK1γ3(h)	87	CK1γ3(h)	2	CSNK1A1(YEAST)	69	CHK1(h)	105	CHK1(h)	105
MAP3K7(h)	12	CHK2(h)	4	CK1β(h)	94	CK1β(h)	35	CSNK1A1(h)	111	CK1β(h)	92	CK1β(h)	92
MAPK9(h)	87	CHK2(H157T)(h)	9	CK2(h)	103	CK2(h)	103	DAPK2(h)	90	CHK2(h)	105	CHK2(h)	105
MAPK1(h)	33	CHK2(R145W)(h)	12	CK2α2(h)	109	CK2α2(h)	90	DAPK3(h)	43	CHK2(H157T)(h)	132	CHK2(H157T)(h)	132
MAPKAPK2(h)	17	CK1γ1(h)	97	ckit(D816H)(h)	14	ckit(D816H)(h)	22	DDR2(h)	107	CK1γ1(h)	90	CK1γ1(h)	90
MAPKAPK5(h)	17	CK1γ2(h)	101	ckit(D816V)(h)	76	ckit(D816V)(h)	92	DMPK(h)	114	CK1γ2(h)	96	CK1γ2(h)	96
MAPKK1(RABBIT)	30	CK1γ3(h)	113	ckit(h)	100	ckit(h)	71	DYRK2(h)	90	CK1γ3(h)	102	CK1γ3(h)	102
MARCK(h)	25	CK1α(h)	105	ckit(V560G)(h)	15	ckit(V560G)(h)	18	EGFR(h)	110	CK1α(h)	109	CK1α(h)	109
MELK(h)	6	CK1β(h)	104	ckit(V654A)(h)	34	ckit(V654A)(h)	34	EGFR(L858R)(h)	105	CK1β(h)	97	CK1β(h)	97
MEK1(h)	28	CK2(h)	112	CLK3(h)	101	CLK3(h)	65	EGFR(L861Q)(h)	99	CLK3(h)	102	CLK3(h)	102
MEK2(h)	71	ckit(D816H)(h)	9	c-RAF(h)	94	c-RAF(h)	94	EPHA2(h)	107	ckit(D816H)(h)	110	ckit(D816H)(h)	110
NEK2(h)	96	ckit(D816V)(h)	93	CSK(h)	107	CSK(h)	82	EPHA3(h)	109	ckit(D816V)(h)	104	ckit(D816V)(h)	104
NEK6(h)	48	ckit(h)	109	cSRC(h)	86	cSRC(h)	14	EPHA4(h)	104	ckit(h)	105	ckit(h)	105
NTRK3(h)	2	ckit(V560G)(h)	9	DAPK1(h)	91	DAPK1(h)	50	EPHA4(h)	94	ckit(V560G)(h)	97	ckit(V560G)(h)	97
P38-ALPHA(h)	51	ckit(V654A)(h)	46	DAPK2(h)	100	DAPK2(h)	85	EPHB2(h)	239	ckit(V654A)(h)	111	ckit(V654A)(h)	111
P38-BETA(h)	25	CLK2(h)	68	DCAMK2(h)	116	DCAMK2(h)	105	EPHB4(h)	106	CLK2(h)	107	CLK2(h)	107
P38-DELTA(h)	46	CLK3(h)	107	DDR2(h)	113	DDR2(h)	57	EPHB4(h)	99	CLK3(h)	99	CLK3(h)	99
P38-GAMMA(h)	46	c-RAF(h)	107	DMPK(h)	94	DMPK(h)	97	ERBB4(h)	103	c-RAF(h)	102	c-RAF(h)	102
PAK1(h)	73	CSK(h)	75	DRAK1(h)	3	DRAK1(h)	15	FER(h)	104	CSK(h)	100	CSK(h)	100
PAK4(h)	78	cSRC(h)	87	DYRK2(h)	97	DYRK2(h)	86	FES(h)	41	cSRC(h)	115	cSRC(h)	115
PDGFRβ(h)	7	DAPK1(h)	82	eEF-2K(h)	106	eEF-2K(h)	93	FGFR1(h)	43	DAPK1(h)	109	DAPK1(h)	109
PKA(h)	0	DAPK3(h)	0	EGFR(h)	109	EGFR(h)	109	FGFR2(h)	114	DAPK3(h)	114	DAPK3(h)	114
PKH_GAMMA1(RABB)	6	DCAMK12(h)	112	EGFR(L858R)(h)	102	EGFR(L858R)(h)	50	FGFR3(h)	102	DCAMK12(h)	109	DCAMK12(h)	109
PI3K(h)	49	DDR2(h)	101	EGFR(L861Q)(h)	117	EGFR(L861Q)(h)	72	FGFR4(h)	99	DDR2(h)	101	DDR2(h)	101
PI3K(h)	36	DMPK(h)	100	EGFR(T790M)(h)	82	EGFR(T790M)(h)	65	FGFR(h)	71	DMPK(h)	94	DMPK(h)	94
PKA(BOVINE)	45	DRAK1(h)	62	EGFR(T790M.L858R)(h)	103	EGFR(T790M.L858R)(h)	68	FLT1(h)	86	DRAK1(h)	121	DRAK1(h)	121
PKC2α(h)	8	DYRK2(h)	102	EphA1(h)	82	EphA1(h)	18	FLT3(h)	25	DYRK2(h)	118	DYRK2(h)	118
PKC2β(h)	21	eEF-2K(h)	115	EphA2(h)	127	EphA2(h)	95	FLT3CD35Y(h)	6	eEF-2K(h)	105	eEF-2K(h)	105
PKC(h)	73	EGFR(h)	116	EphA3(h)	114	EphA3(h)	86	FYNI(h)	71	EGFR(h)	116	EGFR(h)	116
PK3(h)	54	EGFR(L858R)(h)	76	EphA4(h)	100	EphA4(h)	77	GSK3A(h)	107	EGFR(L858R)(h)	101	EGFR(L858R)(h)	101
PRKAA1(h)	5	EGFR(L861Q)(h)	68	EphA5(h)	89	EphA5(h)	90	GSK3B(h)	105	EGFR(L861Q)(h)	98	EGFR(L861Q)(h)	98
PTK2(h)	93	EGFR(T790M)(h)	36	EphA7(h)	131	EphA7(h)	118	HCK(h)	148	EGFR(T790M)(h)	89	EGFR(T790M)(h)	89
RAF(h)	128	EGFR(T790M.L858R)(h)	12	EphA8(h)	106	EphA8(h)	91	HIPK2(h)	105	EGFR(T790M.L858R)(h)	102	EGFR(T790M.L858R)(h)	102
RIPK2(h)	20	EphA1(h)	99	EphB1(h)	101	EphB1(h)	119	IGF1R(h)	145	EphA1(h)	96	EphA1(h)	96
ROCK1(h)	28	EphA2(h)	131	EphB2(h)	103	EphB2(h)	99	IKK_α/PHA(h)	96	EphA2(h)	107	EphA2(h)	107
ROCK2(α)	21	EphA3(h)	111	EphB3(h)	93	EphB3(h)	113	IKK_BETA(h)	109	EphA3(h)	109	EphA3(h)	109
RPS6KA1(α)	10	EphA4(h)	103	EphB4(h)	110	EphB4(h)	83	INSR(h)	103	EphA4(h)	107	EphA4(h)	107
RPS6KA1(h)	68	EphA5(h)	109	ErbB4(h)	127	ErbB4(h)	116	INSR(h)	103	EphA5(h)	127	EphA5(h)	127
RPS6KA5(h)	25	EphA7(h)	102	FAK(h)	80	FAK(h)	76	IRAK4(h)	85	EphA7(h)	118	EphA7(h)	118
RPS9B(h)	17	EphA8(h)	108	Fer(h)	129	Fer(h)	14	ITK(h)	127	EphA8(h)	101	EphA8(h)	101
RPS9K1(T412E)(h)	11	EphB1(h)	104	Fes(h)	96	Fes(h)	14	JAK2(h)	100	EphB1(h)	99	EphB1(h)	99
SGKH(h)	20	EphB2(h)	92	FGFR1(h)	48	FGFR1(h)	4	JAK3(h)	100	EphB2(h)	103	EphB2(h)	103
SGK1(h)	3	EphB3(h)	132	FGFR1(V561M)(h)	9	FGFR1(V561M)(h)	6	JNK1A1(h)	106	EphB3(h)	107	EphB3(h)	107
SRC(h)	94	EphB4(h)	137	FGFR2(h)	86	FGFR2(h)	65	JNK3(h)	110	SRC(h)	104	SRC(h)	104
TIE2(h)	105	EphB4(h)	102	FGFR2(N549H)(h)	50	FGFR2(N549H)(h)	11	KDR(h)	95	EphB4(h)	90	EphB4(h)	90
TOPK(h)	10	FAK(h)	75	FGFR3(h)	88	FGFR3(h)	25	KIT(h)	112	FAK(h)	129	FAK(h)	129
ZAP70(h)	117	Fer(h)	6	FGFR4(h)	113	FGFR4(h)	44	Kiit(D816V)(h)	107	Fer(h)	102	Fer(h)	102
		Fes(h)	92	Fgr(h)	97	Fgr(h)	44	LCK(h)	82	Fes(h)	120	Fes(h)	120
		FGFR1(h)	29	FR1(h)	14	FR1(h)	6	LIMK1(h)	120	FGFR1(h)	103	FGFR1(h)	103
		FGFR1(V561M)(h)	73	FR3(D835Y)(h)	2	FR3(D835Y)(h)	10	LYN(h)	99	FGFR1(V561M)(h)	98	FGFR1(V561M)(h)	98
		FGFR2(h)	56	FR3(h)	9	FR3(h)	8	LYN(m)	67	FGFR2(h)	122	FGFR2(h)	122
		FGFR2(N549H)(h)	25	FR4(h)	13	FR4(h)	1	MAP2K1(h)	99	FGFR2(N549H)(h)	96	FGFR2(N549H)(h)	96
		FGFR3(h)	60	Fms(h)	60	Fms(h)	17	MAP2K2(h)	106	FGFR3(h)	106	FGFR3(h)	106
		FGFR4(h)	105	Fyn(h)	86	Fyn(h)	114	MAP2K7(h)	103	FGFR4(h)	92	FGFR4(h)	92
		Fgr(h)	57	GCK(h)	13	GCK(h)	17	MAP3K5(h)	117	Fgr(h)	106	Fgr(h)	106
		FR1(h)	28	GRK5(h)	109	GRK5(h)	114	MAP3K7(h)	56	FR1(h)	122	FR1(h)	122
		FR3(D835Y)(h)	9	GRK6(h)	100	GRK6(h)	108	MAPK1(m)	90	FR3(D835Y)(h)	108	FR3(D835Y)(h)	108
		FR3(h)	43	GSK3β(h)	86	GSK3β(h)	118	MAPK11(h)	107	FR3(h)	99	FR3(h)	99
		Frs(h)	2	GSK3α(h)	88	GSK3α(h)	99	MAPK12(h)	109	Frs(h)	95	Frs(h)	95
		Fms(h)	60	Hsp90(h)	87	Hsp90(h)	0	MAPK13(h)	97	Fms(h)	100	Fms(h)	100
		Fyn(h)	79	Hck(h)	99	Hck(h)	63	MAPK14(h)	94	Fyn(h)	103	Fyn(h)	103
		GCK(h)	44	HIPK1(h)	82	HIPK1(h)	78	MAPK2K4(m)	95	GCK(h)	109	GCK(h)	109
		GRK3(h)	122	HIPK2(h)	93	HIPK2(h)	63	MAPK3(h)	89	GRK3(h)	107	GRK3(h)	107
		GRK6(h)	101										

**Table S1. Kinase Selectivity Data for PDK1 Inhibitors**

Kinase	Cmpd 1 [10 μM]		Cmpd 2 [1 μM]		Cmpd 3 [1 μM]		Cmpd 4 [10 μM]		Cmpd 5 [1 μM]		Cmpd 6 [1 μM]		Cmpd 7 [10 μM]		
	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	% Activity	Kinase	
		MKK7(h)	107	MSSK1(h)	113	MSSK1(h)	58	PKO2(h)	78						
		MLCK(h)	53	MST1(h)	102	MST1(h)	40	PLK2(h)	102					MNK(h)	113
		MLK1(h)	1	MST2(h)	119	MST2(h)	104	PLK3(h)	95					MKK4(m)	112
		Mnk2(h)	30	MST3(h)	195	MST3(h)	106	PRAK(h)	80					MKK6(h)	115
		MRCR(h)	111	MuSK(h)	89	MuSK(h)	99	PRKD2(h)	56					MKK7(h)	95
		MRCR(h)	99	NEK11(h)	117	NEK11(h)	51	PRKG1(h)	95					MLCK(h)	110
		MSSK1(h)	83	NEK2(h)	93	NEK2(h)	80	PTK2(h)	21					MLK1(h)	91
		MSSK2(h)	61	NEK3(h)	99	NEK3(h)	88	PTK6(h)	93					Mnk2(h)	101
		MSSK1(h)	115	NEK6(h)	114	NEK6(h)	109	PTPN7(h)	110					MRCR(h)	101
		MST1(h)	30	NEK7(h)	109	NEK7(h)	121	RAF1(h)	106					MRCR(h)	101
		MST2(h)	60	NLK(h)	58	NLK(h)	78	RET(h)	37					MSK1(h)	109
		MST3(h)	125	p70S6K(h)	85	p70S6K(h)	0	RIPK2(h)	93					MSSK2(h)	106
		mTOR(h)	89	PAK2(h)	111	PAK2(h)	98	ROCK1(h)	66					MSSK1(h)	114
		mTOR-FKBP12(h)	94	PAK3(h)	106	PAK3(h)	38	ROCK2(h)	87					MST1(h)	103
		MuSK(h)	96	PAK4(h)	99	PAK4(h)	106	ROCK2(r)	88					MST2(h)	101
		NEK1(h)	116	PAK5(h)	115	PAK5(h)	121	ROS1(h)	95					MST3(h)	100
		NEK2(h)	116	PAK6(h)	145	PAK6(h)	112	RPS8A1(h)	2					mTOR(h)	102
		NEK3(h)	104	PAR-1B(a)	9	PAR-1B(a)	108	RPS8A1(r)	6					mTOR-FKBP12(h)	103
		NEK4(h)	110	PASK(h)	103	PASK(h)	4	RPS8KA2(h)	2					MuSK(h)	98
		NEK7(h)	111	PDGFR(h)	97	PDGFR(h)	77	RPS8KA3(h)	2					NEK11(h)	126
		NLK(h)	85	PDGFR(D842V)(h)	-6	PDGFR(D842V)(h)	5	RPS8KA4(h)	43					NEK2(h)	94
		p70S6K(h)	45	PDGFR(r)	86	PDGFR(r)	79	RPS8KA5(h)	68					NEK3(h)	104
		PAK2(h)	99	PDGFR(V561D)(h)	14	PDGFR(V561D)(h)	10	RPS8KB1(h)	76					NEK6(h)	99
		PAK3(h)	78	PDK1(h)	5	PDK1(h)	43	SGK(h)	77					NEK7(h)	102
		PAK4(h)	95	Phk2(h)	74	Phk2(h)	33	SGK2(h)	70					NLK(h)	100
		PAK5(h)	103	Pim-1(h)	103	Pim-1(h)	3	SGK3(h)	94					p70S6K(h)	108
		PAK6(h)	103	Pim-2(h)	91	Pim-2(h)	24	SNF1L(h)	18					PAK2(h)	94
		PAR-1B(b)	87	Pim-3(h)	116	Pim-3(h)	22	SRG(h)	104					PAK3(h)	88
		PASK(h)	109	PKA(h)	77	PKA(h)	51	SRPK1(h)	106					PAK4(h)	105
		PDGFR(D842V)(h)	1	PKB(h)	98	PKB(h)	15	SRPK2(h)	108					PAK5(h)	100
		PDGFR(r)	74	PKB(a)	103	PKB(a)	25	STK10(h)	81					PAK6(h)	101
		PDGFR(V561D)(h)	1	PKC(h)	103	PKC(h)	26	STK11(h)	104					FAK1-1(h)	96
		PDGFR(h)	102	PKC(a)	53	PKC(a)	32	STK17A(h)	23					PASK(h)	111
		PDK1(h)	2	PKC(b)	72	PKC(b)	99	STK23(h)	90					PDGFR(D842V)(h)	108
		Phk2(h)	76	PKC(β)(h)	106	PKC(β)(h)	118	STK3(h)	69					PDGFR(r)	108
		Pim-1(h)	107	PKC(γ)(h)	88	PKC(γ)(h)	94	STK4(h)	32					PDGFR(V561D)(h)	112
		Pim-2(h)	99	PKC(δ)(h)	96	PKC(δ)(h)	88	SYK(h)	65					PDGFR(h)	113
		Pim-3(h)	96	PKC(ε)(h)	84	PKC(ε)(h)	134	TBK1(h)	59					PDGFR(h)	17
		PKA(h)	106	PKC(ζ)(h)	84	PKC(ζ)(h)	81	TEK(h)	106					Phk2(h)	101
		PKB(a)	98	PKC(η)(h)	107	PKC(η)(h)	85	TRKA(h)	46					Pim-1(h)	104
		PKB(b)	90	PKC(θ)(h)	95	PKC(θ)(h)	95	TSSK1(h)	24					Pim-2(h)	100
		PKB(γ)(h)	102	PKC(ι)(h)	103	PKC(ι)(h)	57	TSSK2(h)	56					Pim-3(h)	97
		PKC(a)	108	PKC(j)(h)	121	PKC(j)(h)	107	TYRO3(h)	111					PKA(h)	113
		PKC(b)	94	PKD2(h)	75	PKD2(h)	15	WNK3(h)	111					PKB(h)	107
		PKC(H)(h)	105	PKG1(h)	100	PKG1(h)	34	YES1(h)	77					PKB(h)	107
		PKC(i)	95	PKG1(a)	107	PKG1(a)	29	ZAP70(h)	114					PKB(β)(h)	99
		PKC(k)	79	Plk3(h)	111	Plk3(h)	110							PKC(a)	98
		PKC(l)	106	PRAK(h)	78	PRAK(h)	50							PKC(β)(h)	95
		PKC(m)	108	PRK2(h)	63	PRK2(h)	13							PKC(β)(h)	96
		PKC(n)	109	PRK4(h)	70	PRK4(h)	91							PKC(γ)(h)	104
		PKC(O)(h)	78	PTK5(h)	93	PTK5(h)	90							PKC(δ)(h)	105
		PKC(p)	98	Pyk2(h)	85	Pyk2(h)	47							PKC(ε)(h)	96
		PKC(q)	86	Ret(h)	30	Ret(h)	9							PKC(ζ)(h)	106
		PKD2(h)	96	RIPK2(h)	111	RIPK2(h)	78							PKC(η)(h)	96
		PKG1(a)	97	ROCK-I(h)	96	ROCK-II(h)	46							PKC(θ)(h)	108
		PKI1(h)	81	ROCK-III(h)	59	ROCK-III(h)	67							PKC(ι)(h)	97
		Plk3(h)	85	Rorb(h)	106	Rorb(h)	106							PKC(j)(h)	100
		PRAK(h)	75	Rorb(h)	117	Rorb(h)	54							PKD2(h)	110
		PRK2(h)	10	Rse(h)	84	Rse(h)	19							PKG1(h)	111
		PRK3(h)	103	Rsk1(h)	83	Rsk1(h)	13							PKG1(h)	108
		PRK4(h)	92	Rsk2(h)	118	Rsk2(h)	24							PKI1(h)	116
		PRK5(h)	59	Rsk3(h)	120	Rsk3(h)	8							PKI3(h)	96
		Ret(V804L)(h)	2	Rsk4(h)	103	Rsk4(h)	15							PKA(h)	98
		Ret(h)	1	SAPK2a(h)	108	SAPK2a(h)	72							PRK2(h)	96
		Ret(V804M)(h)	13	SAPK2a(T106M)(h)	95	SAPK2a(T106M)(h)	79							PRK2(h)	107
		RIPK2(h)	51	SAPK2b(h)	85	SAPK2b(h)	81							PRK3(h)	96
		ROCK-I(h)	102	SAPK3(h)	98	SAPK3(h)	85							PTK5(h)	106
		ROCK-II(h)	29	SAPK4(h)	115	SAPK4(h)	43							Pyk2(h)	98
		Rorb(h)	98	SGK(h)	70	SGK(h)	19							Ret(V804L)(h)	112
		Rorb(h)	98	SGK2(h)	94	SGK2(h)	26							Ret(V804M)(h)	109
		Rse(h)	94	SGK3(h)	81	SGK3(h)	12							RIPK2(h)	101
		Rsk1(h)	20	SIK(h)	12	SIK(h)	25							ROCK-I(h)	97
		Rsk2(h)	5	Snk(h)	112	Snk(h)	107							ROCK-II(h)	109
		Rsk3(h)	7	SRPK1(h)	100	SRPK1(h)	80							Rorb(h)	82
		Rsk4(h)	12	SRPK2(h)	99	SRPK2(h)	96							Rorb(h)	111
		SAPK2a(h)	107	STK33(h)	82	STK33(h)	58							Rse(h)	118
		SAPK2a(T106M)(h)	103	Syk(h)	66	Syk(h)	33							Rsk1(h)	107
		SAPK2b(h)	110	TAK1(h)	32	TAK1(h)	83							Rsk2(h)	124
		SAPK3(h)	106	TAK2(h)	37	TAK2(h)	81							Rsk3(h)	102
		SAPK4(h)	108	TAK3(h)	10	TAK3(h)	66							Rsk4(h)	113
		SGK(h)	74	TBK1(h)	12	TBK1(h)	47							SAPK2a(h)	107
		SGK2(h)	86	Tec2(h)	95	Tec2(h)	5							SAPK2a(T106M)(h)	113
		SGK3(h)	104	TLK2(h)	91	TLK2(h)	106							SAPK2b(h)	100
		SIK(h)	23	TrkA(h)	31	TrkA(h)	4							SAPK3(h)	115
		Snk(h)	72	TrkB(h)	42	TrkB(h)	23							SAPK4(h)	114
		Src(1-530)(h)	83	TSSK1(h)	99	TSSK1(h)	99							SGK(h)	106
		Src(1341M)(h)	55	TSSK2(h)	52	TSSK2(h)	72							SGK2(h)	97
		SRPK1(h)	104	VRK2(h)	117	VRK2(h)	115							SGK3(h)	117
		SRPK2(h)	107	Wnk2(h)	95	Wnk2(h)	65							SIK(h)	102
		STK33(h)	41	Wnk3(h)	108	Wnk3(h)	104							Sak(h)	97
		Syk(h)	105	Yes(h)	110	Yes(h)	109							Src(1-530)(h)	94
		TAK1(h)	90	ZAP-70(h)	120	ZAP-70(h)	99							Src(1341M)(h)	102
		TAK2(h)	95	ZIPK(h)	102	ZIPK(h)	34							SRPK(h)	104
		TAK3(h)	101											SRPK(h)	102
		TBK1(h)	78											STK33(h)	104
		Tec2(h)	109											Syk(h)	102
		Tec2(R849W)(h)	74											TAK1(h)	101
		Tec2(Y897S)(h)	82											TAK2(h)	96
		TLK2(h)	80											TAK3(h)	100
		TrkA(h)	10											Tec(h) activated	91
		TrkB(h)	59											Tec2(h)	105
		TSSK1(h)	75											Tec2(R849W)(h)	104
		TSSK2(h)	106											Tec2(Y897S)(h)	111
		TrkA(h)	84											TLK2(h)	100
		TLK2(h)	30											TrkA(h)	108
		TLK3(h)	47											TrkB(h)	95
		VRK2(h)	111											TSSK1(h)	100
		Wnk2(h)	98											TSSK2(h)	115
		Wnk3(h)	73											Trk(h)	138
		Yes(h)	65											TLK2(h)	110
		ZAP-70(h)	104											TLK3(h)	99
		ZIPK(h)	57											VRK2(h)	99
														Wnk2(h)	104
														Wnk3(h)	99
														Yes(h)	91
														ZAP-70(h)	100
														ZIPK(h)	121

## Supplementary Figure legends

### **Supplementary Figure S1. Dose dependent toxicity of GeneBloc antisense RNA lipid transfection reagent.**

PC-3 cells were transfected with PDK1 targeting GeneBloc antisense RNA (GB) or a scrambled mismatch control RNA (mm) using increasing concentration of lipid in the transfection mixture. Cell viability was determined at 72 hours post-transfection by ATP ViaLight.

### **Supplementary Figure S2. Optimization of PDK1 knockdown in PC-3 cells shows potent pathway inhibition but has minimal effect on cell proliferation.**

**(a)** Thirty independent shRNA sequences were tested for their PDK1 knockdown potential. Quantitative PCR for PDK1 was performed for each shRNA 48 hours after transfection and is represented as a percentage of total PDK1 mRNA in non transfected control cells. Arrows indicate the greatest degree of target mRNA knockdown. **(b)** A pool of stably transduced PC-3 cells containing doxycycline-inducible PDK1 shRNA coupled to GFP expression was incubated with doxycycline and analyzed for GFP expression by flow cytometry. Arrow indicates a population of stably transduced cells, based on antibiotic selection, which fail to successfully induce GFP (and therefore PDK1 shRNA) upon doxycycline treatment. **(c)** PC-3 cells, expressing tet-KRAB, were transduced with either of two independent PDK1 shRNAs (sh3 and sh20) were subcloned, grown in the absence or presence of doxycycline, and analyzed for PDK1 protein knockdown and downstream signaling effects. **(d)** Representative cell proliferation assays of isogenic PC-3 subclones (analyzed in part c) grown in the absence or presence of doxycycline.