## Biological specificity of CDK4/6 inhibitors: dose response relationship, in vivo signaling, and composite response signature

## **Supplementary Material**

ienes where p < 0.1 for MCF7 and T47D for both PD and LY (n = 599)

	MCF7		T47D		M CF7/T47D Comparison			
	Upregulated	Downregulated	Upregulated	Downregulated	Upregulated Concordance	Downregulated Concordance	Overall Concordance	
PD	221	378	271	328	73.24%	80.5 6%	87.31%	
LY	231	368	238	361	9 0.65%	93.88%	96.16%	
Concordance (PD/LY)	82.26%	88.86%	69.10%	76.21%				
Overall Concordance (PD /I V)	07	E E Ro	24 47 %					

LY downregulated GO biological process complete	GD Term	Homo saplens - REFUST (20972)	upload 1(950)	upload 1(expected)	upload 1(over/under)	upload 1 (fold Enrichment)	upload 1 (P-value)
cell cycle	GD:0007049	1337	272	46.41	+	5.86	1.47E-127
cell cycle process	GD:0022402	1091	244	37.87	I	544	4.19E-121
mitotic cell cucle	GD:00022402	794	209	27.56	I	758	1.45E-114
mitotic cell cycle process	GD:1903047	766	205	26.59	I	771	1.99E-113
nuclear division	GD:0000280	518	150	17.98	I	834	9.34E-85
organelle fission	GD:0048285	549	151	19.06		792	2.46E-82
	GD:0048283	385		13.36	•		
mitotic nuclear division		383 1012	126 186	13.36 35.13	•	9.43 5.29	4.08E-76
chromosome organization	GD:0051276				•		4.83E-75
DNA metabolic process	GD:0006259	781	159	27.11	•	5.86	7.85E-69
cell division	GD:0051301	476	128	16.52	•	7.75	1.42E-67
LY upregulated							
GO biological process complete	GD Term	Homo saplens - REFLIST (20972)	upload_1 (550)	upload_1(expected)	upload_1(over/under)	upload_1 (fold Enrichment)	upload_1 (P-value)
G-protein coupled receptor signaling paths	wa GD:0007186	1193	3	31.29	-	< 0.2	5.38E-07
small molecule metabolic process	GD:0044281	1768	92	46.37	+	198	2.22E-06
organonitrogen compound metabolic proc	us GD:1901564	1835	91	48.12	•	189	2.99E-05
organic substance databolic process	GD:1901575	1594	79	41.8	•	1.89	3.92E-04
catabolic process	GD:0009056	1886	89	49.46	•	1.8	4.44E-04
single-organism metabolic process	GD:0044710	3544	142	92.94	•	153	7.14E-04
cellular databolic process	GD:0044248	1581	77	41.46	•	186	1.19E-03
organic acid metabolic process	GD:0006082	956	54	25.07		2.15	1.34E-03
oxoacid metabolic process	GD:0043436	939	53	24.63		215	1.80E-03
monocarboxylic acid metabolic process	GD:0032787	508	35	13.32		2.63	3.04E-03
carboxylic acid metabolic process	GD:0019752	832	48	21.82		2.2	3.77E-03

Supplementary Figure 1: Genes where p < 0.1 for MCF7 and T47D for both PD and LY (n = 599).

## Genes where p < 0.1 for MCF7 and T47D for both PD and LY (n = 599).

	MB468 Comparison			
	Overall Concordance w/MCF7	Overall Concordance w/T47D		
PD	54.59%	49.25%		
LY (250uM LY)	53.92%	53.09%		

LY upregulated							
GO biological process complete	60 Term	Homo sepiens - REFLIST (20972)	upload_1 (463)	upload_1 (expected)	upload_1 (over/under)	upload_1 (fold Enrichment)	upload_1 (P-value)
ncRNA processing	0.0:0034470	392	35	8.65	•	5.81	9.806-07
ncRNA metabolic process	0.0:0034660	545	39	12.05	+	5.24	2.07 €-06
metabolic process	0.0:0008152	9790	274	216.13	•	1.27	5.77 E-04
ribosome biogenesis	G O:0042254	517	25	7	+	3.57	6.208-04
rRNA processing	0.0:0006364	257	22	5.67	+	3.55	9.628-04
rffNA metabolic process	G O:0016072	252	25	6.23		3.69	1.166-05
RNA processing	G C:0006596	265	45	19.16		2.55	1.546-05
mitochondrial transport	C 0:0006839	2 29	20	5.06		3.96	2.656-05
collular metabolic process	G O:0044 2 57	5525	248	194.79		1.27	3.456-05
single-organism metabolic process	50:0044710	3544	119	78.24	+	1.52	9.356-05
ribosomal large subunit biogenesis	GO:0042275	61	10	1.55	+	7.43	1.228-02
LY downregulated							
LY downregulated GO biological process complete	60 Term	Homo sepiens - REFLIST (20972)	upload_1 (739)	upload_1 (expected)	upload_1 (over/under)	upload_1 (fold Enrichment)	upload_1 (P-value)
	60 Term 50:0065007	Homo sapiers - REFLIST (20972) 11695	upbed_1 (799) 505	upload_1 (expected) 412.05	upload_1 (over/under) +	uplosd_1 (fold Enrichment) 125	upload_1 (P-value) 2.765-09
60 biological process complete				-,,	upload_1 (over/under) + +		
60 biological process complete biological regulation	G:0:0065007	11695	508	412.03	upload_1 (over/under) + + +	125	2.768-09
GO biological process complete biological regulation regulation of collular process	G 0:0065007 G 0:0050794	11695 10465	508 462	412.05 365.69	uplosd_1 (over/under) + + + + +	125 125	2.766-09 2.776-05
GO biological process complete biological regulation regulation of cellular process regulation of biological process	G 0:005507 G 0:0050794 G 0:0050789	11695 10465 11075	508 462 478	412.05 365.69 390.25	uplosd_1 (over/under) + + + + + +	125 125 122	2.768-09 2.778-05 3.578-07
GO biological process complete biological regulation regulation of collular process regulation of biological process positive regulation of collular process	G 0:0065007 G 0:0050794 G 0:0050789 G 0:0045522	11695 10465 11075 4774	508 462 478 245	412.05 565.69 590.25 165.22	uplosd_1 (over/under) + + + + + + +	125 125 122 146	2.765-09 2.775-05 3.575-07 6.045-07
GO biological process complete biological regulation regulation of colular process regulation of biological process regulation of biological process regulation of biological process regulation of biological process	G 0:0065007 G 0:0050794 G 0:0050789 G 0:0045522 G 0:0045519	11695 10465 11075 4774 4757	505 462 475 245 241	412.05 365.69 390.25 165.22 166.92	upload_1 (over/under) + + + + + + + + + +	125 125 122 146 144	2.768-09 2.778-06 3.578-07 6.048-07 2.268-06
GO biological process complete biological regulation of culular process regulation of culular process regulation of biological process positive regulation of cirillar process negative regulation of biological process positive regulation of biological process	GC:0065007 GC:0050794 GC:0050789 GC:0045522 GC:0045519 GC:0045515	11695 10465 11075 4774 4737 5321	505 462 478 245 241 262	412.05 555.69 590.25 165.22 166.92 187.5	uplosd_1(over/under) + + + + + + + + + + + + +	125 125 122 146 144	2.768-09 2.778-05 5.578-07 6.048-07 2.268-06 6.408-06
GO biologícal procesa complete biological regulation regulation of colular procesa regulation of biological procesa regulation of biological procesa regulation of obliogical procesa positive regulation of biological procesa positive regulation of biological procesa regulation of colular procesa	C:006507 C:0050794 C:0050789 C:0050789 C:0045522 C:0045519 C:0045515 C:0045525	11695 10465 11075 4774 4757 5321 4261	505 462 475 245 241 262 217	412.05 565.69 590.25 165.22 166.92 187.5 150.15	uplosd_1(over/under) + + + + + + + + + + + + + + + +	125 125 122 146 144 1.4	2.768-09 2.778-05 5.578-07 6.048-07 2.268-06 6.408-05 2.748-05
GO biological process complete biological regulation of colular process regulation of colular process regulation of biological process positive regulation of biological process positive regulation of biological process positive regulation of biological process negative regulation of biological process negative regulation of colular process biological_process	C.0008507 C.00050794 C.00050789 C.00045522 C.00045519 C.00045516 C.00045536	11 6 95 10 4 65 11 0 75 4 77 4 4 75 7 5 32 1 4 20 1 1 7 2 40	508 462 478 245 241 262 217 663	412.05 368.69 390.25 188.22 186.92 187.5 190.15	uplosd_1(over/under) + + + + + + + + + + + + + + + + +	125 125 122 146 144 1.4 145	2.768-09 2.778-05 3.578-07 6.048-07 2.268-06 6.408-06 2.748-05 6.918-05
GO biological process complete biological regulation of calular process regulation of calular process regulation of biological process positive regulation of calular process positive regulation of biological process positive regulation of biological process negative regulation of biological process biological_process regulation of motabolic process regulation of motabolic process	C::006507 C::0050794 C::0050799 C::0048522 C::0048519 C::0048515 C::0048515 C::0048515	11625 10465 11075 4774 4757 5521 4261 17240 6550	505 462 478 245 241 262 217 663 293	412.03 385.89 390.25 185.22 186.92 187.5 190.13 607.49 224.51	upload_1(over/under) + + + + + + + + + + + + + + + + + + +	125 125 122 146 144 14 145 109	2,768-09 2,778-05 5,578-07 6,048-07 2,268-06 6,408-06 2,748-05 6,918-05 5,058-04
GO biologícal procesa complete biological regulation of colular procesa regulation of colular procesa regulation of biological procesa negative regulation of biological procesa negative regulation of biological procesa positive regulation of biological procesa positive regulation of biological procesa biological procesa biological procesa regulation of octuber procesa regulation of octuber mediabolic procesa regulation of colular mediabolic procesa	G 0.0065007 G 0.00507 24 G 0.00507 29 G 0.0045522 G 0.0045512 G 0.0045512 G 0.0045512 G 0.0045522 G 0.005150	11695 10465 11075 4774 4757 5321 4261 17240 6350 5950	505 462 475 245 241 262 217 663 295 276	412.05 555.69 500.25 165.22 166.92 187.5 180.15 607.49 224.51 209.66	uplosd_1(over/under) + + + + + + + + + + + + + + + + + + +	125 125 122 146 144 1.4 145 109 1.5	2.765-08 2.775-05 3.575-07 6.045-07 2.265-06 6.405-06 2.745-05 6.915-05 5.055-04 6.765-04

Supplementary Figure 2: Genes where p < 0.1 for MCF7 and T47D for both PD and LY (n = 599).

In vivo - p < 0.1 for both PD and LY (n = 2109)

	In vivo		
	Upregulated	Downregulated	
PD	914	1195	
LY	916	1193	
Concordance (PD/LY)	93.86%	95.26%	
Overall Concordance (PD/LY)	97.25%		

LY/PD downregulated							
GO biological process complete	GOTerm	Homo saplens - REFLIST (20972)	upload_1 (540)	upload_1 (expected)	upload_1 (over/under)	upload_1 (fold Enrichment)	upload_1 (P-value)
cell cycle	G0:0007049	1337	177	34.43	•	5.14	8.07E-72
mitotic cell cycle	GO:0000278	794	137	20.44	•	6.7	6.96E-67
cell cycle process	G0:0022402	1091	156	28.09	•	5.55	2.25E-66
mitotic cell cycle process	GO:1903047	766	134	19.72	•	6.79	6.18E-66
chromosome organization	GO:0051276	1012	129	26.06	•	4.95	7.60E-48
mitotic nuclear division	GO:0007067	385	84	9.91	•	8.47	3.10E-45
nuclear division	GO:0000280	518	93	13.34	•	6.97	1.07E-44
organelle fission	G0:0048285	349	95	1414	•	6.72	1.95E-44
DNA metabolic process	GO:0006259	781	107	20.11	•	5.32	2.15E-41
chromosome segregation	GO:0007059	295	70	7.6	•	9.22	3.94E-40
organelle organization	GO:0006996	3186	213	82.04	•	2.6	1.48E-38
cell division	G0:0051301	476	82	12.26	•	6.69	1.44E-37
DNA replication	GO:0006260	217	59	5.59	•	10.56	1.97E-36
nuclear chromosome segregation	G0:0098813	254	62	6.54	•	9.48	8.19E-36
sister chromatid segregation	G0:0000819	183	53	4.71	•	11.25	9.98E-34
cell cycle phase transition	GO:0044770	268	60	6.9	•	8.69	1.64E-32
mitotic cell cycle phase transition	G0:0044772	262	59	6.75	•	8.75	4.76E-32
LY/PD upregulated							
GO biological process complete	GOTerm	Homo sapiens - REFLIST (20972)	upload_1 (303)	upload_1 (expected)	upload_1 (over/under)	upload_1 (fold Enrichment)	upload_1 (P-value)
single-organism cellular process	G0:0044763	9816	190	141.82	+	1.34	1.57E-04
single-organism metabolic process	G0:0044710	3544	89	51.2	+	1.74	4.41E-04
organophosphate biosynthetic process	G0:0090407	496	23	7.17	+	3.21	1.08E-02
carbohydrate derivative biosynthetic process	GO:1901137	596	25	8.61	+	2.9	2.17E-02
basement membrane organization	G0:0071711	15	5	0.22	+	23.07	2.65E-02
lipid metabolic process	GO:0006629	1234	39	1783	+	2.19	3.64E-02

Supplementary Figure 3: In vivo- p < 0.1 for both PD and LY (n = 2109).