

## Supplemental Tables

Gene	1 (Up in AD80) / 2 (Low in AD30)	Log2 Fold change	Gene	1 (Up in AD80) / 2 (Low in AD30)	Log2 Fold change	Gene	1 (Up in AD80) / 2 (Low in AD30)	Log2 Fold change
G6PC	1	8.262795	SYT8	1	3.826244	SPATA9	1	3.10268
ADH1B	1	7.508264	ADH4	1	3.800391	SPTSSB	1	3.093815
RNU1-70P	1	6.596403	WNT8B	1	3.799741	CYP26A1	1	3.093672
CYP7A1	1	6.56167	TNFSF10	1	3.795007	ACR	1	3.092358
ADH1A	1	6.358759	HMGCS2	1	3.791218	DUOX2	1	3.090622
SLC2A2	1	6.05681	GNAT1	1	3.737262	SPTLC3	1	3.086353
TNFRSF14-AS1	1	6.055208	CFHR4	1	3.732386	FER1L5	1	3.081569
IGFALS	1	5.825777	BSND	1	3.718276	RASA4CP	1	3.080765
LINC00957	1	5.727226	TSPOAP1	1	3.709555	DOC2GP	1	3.057021
TTBK1	1	5.724558	SLC22A7	1	3.698323	VAT1L	1	3.051293
CYP3A43	1	5.674953	AOC4P	1	3.68655	FMO3	1	3.031314
UGT1A9	1	5.643359	HNF4A-AS1	1	3.679788	SFRP5	1	3.016623
APOL3	1	5.448612	FHAD1	1	3.665007	RFX6	1	3.015833
VCAM1	1	5.442271	ADAMTS10	1	3.61034	SLC5A8	2	3.015901
BFSP2	1	5.396028	NUDT13	1	3.562774	LFNG	2	-3.01667
C22orf31	1	5.349548	FYTTD1P1	1	3.544783	CXCR4	2	-3.0544
FOXN1	1	5.19046	CHAD	1	3.534052	GPR3	2	-3.099
A2MP1	1	5.186347	IRF5	1	3.517716	PA2G4P6	2	3.103813
UROC1	1	5.056845	GSTA7P	1	3.504839	PRDM8	2	3.140796
XAF1	1	5.053767	CXCL10	1	3.486513	DGKG	2	3.261431
ADAMTS14	1	5.049252	SERPINA2	1	3.481204	BCAN	2	3.389266
UGT1A8	1	5.048674	WDR93	1	3.475799	MMP10	2	3.411248
TTLL11-IT1	1	4.965854	MAP6	1	3.465613	MYBPC3	2	3.492397
HRC	1	4.853162	MOV10L1	1	3.457172	MUC12	2	-3.55192
MOGAT2	1	4.797347	HP	1	3.456436	FGF18	2	3.551928

SEPT7P9	1	4.735573	MT1B	1	3.43852	MYO1G	2	- 3.623007
RAB20	1	4.724476	CASR	1	3.414598	ANKRD61	2	- 3.631953
THAP12P5	1	4.722978	PKLR	1	3.406793	CLIC1P1	2	- 3.773794
ANGPTL1	1	4.713348	PRR18	1	3.406115	SPRY4	2	- 3.779795
FGL2	1	4.703365	LHX9	1	3.399799	SERPINE1	2	- -3.88183
ALDOB	1	4.690513	HSD3BP4	1	3.398646	CASC19	2	- 3.936024
ADRA2A	1	4.672076	SORCS3	1	3.397736	IL11	2	- -3.95162
DSEL	1	4.670563	LINC01482	1	3.381454	RASL10A	2	- 3.956945
RARRES3	1	4.667278	LINC01948	1	3.376557	LRRC36	2	- 3.995257
CYP3A7	1	4.666613	SIM1	1	3.375678	IRF6	2	- 4.030169
NPR1	1	4.60485	ARHGAP4	1	3.351453	KRT8P22	2	- 4.154856
TBPL2	1	4.584333	S1PR1	1	3.346809	SRP72P2	2	- 4.155968
CPS1	1	4.535074	GNG5P2	1	3.339409	CCDC158	2	- 4.162351
GLULP3	1	4.486344	MAT1A	1	3.336921	KRT23	2	- -4.18144
ACOT12	1	4.483677	ABCC9	1	3.316358	RERG	2	- 4.263313
LINC01900	1	4.472706	PLG	1	3.315311	BCRP2	2	- 4.288376
ASTN2- AS1	1	4.421647	TRHDE- AS1	1	3.302828	SLC12A9- AS1	2	- 4.290656
LINC00671	1	4.330812	SCARA5	1	3.277119	SCOCP1	2	- 4.406725
COL6A4P2	1	4.315634	DPYS	1	3.266763	PKD1L2	2	- 4.407059
CASP16P	1	4.23705	INHBC	1	3.24724	KRT8P25	2	- 4.407511
CHRNE	1	4.232659	BBOX1	1	3.22843	KRT8P1	2	- -4.40821
FUZ	1	4.202595	C8B	1	3.215234	C9orf84	2	- 4.409531
C1orf141	1	4.198172	PLIN5	1	3.209913	PTPN2P1	2	- -4.41104
CYP8B1	1	4.194463	ITIH1	1	3.193375	EBF1	2	- 4.412159
ADH1C	1	4.14962	RORB	1	3.18897	KLHDC7A	2	- 4.418122

ITIH3	1	4.123324	LINC02068	1	3.186516	IFIT1P1	2	- 4.425365
CYP1B1-AS1	1	4.115127	S100A1	1	3.185405	HCAR2	2	- 4.626337
KLHL1	1	4.06833	LINC02499	1	3.164759	SYN3	2	- 4.647241
AOX3P	1	4.057007	C6	1	3.162615	SLC27A6	2	- 4.826887
PKHD1L1	1	3.965088	MLXIPL	1	3.153884	SBSPON	2	- 4.838843
LPA	1	3.961606	FTCD	1	3.143456	SHC3	2	- 4.921064
CYP3A4	1	3.945235	BGLAP	1	3.141819	MEOX2	2	- 5.005146
C2orf54	1	3.931918	HOGA1	1	3.137846	CRISP3	2	- 5.160243
IP6K3	1	3.928574	LINC01767	1	3.129923	PTPN7	2	- 5.184175
GSN-AS1	1	3.921159	C4A	1	3.12356	CGA	2	- 5.334937
CFHR2	1	3.889435	GOLGA2P5	1	3.119704	PPY	2	- 5.352692
APCS	1	3.881737	DPEP1	1	3.119402	OTOF	2	- 5.533359
ALDH1L1	1	3.860795	CLEC14A	1	3.11721	LINC01121	2	- 5.587001
ACTL7B	1	3.83416	CD22	1	3.114028	L1CAM	2	- 5.742864
CFHR1	1	3.826663	ROBO2	1	3.106367			

**Supplemental Table 1: AD80 signature genes from RNA-seq experiments that were used for Kaplan Meier and Box Plots.**

Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM	Kinase	AD80 1µM
ABL, ARG	51.0	CDK9	1.6	FRAP	-12.6	KHS2	60.3	MAST1, MAST2	6.6	p38a	-11.7	PKN1	5.9	SRPK1	-5.3
ABL, ARG	22.0	CHED	23.6	FRK	51.5	KSR1, KSR2	6.1	MAST3	3.5	p38d, p38g	71.2	PKN2	2.3	SRPK1, SRPK2	3.6
ACK	7.6	CHK1	-23.4	FRK	25.4	LATS1	6.7	MAST4	-1.4	p70S6K	-3.0	PKR	-2.3	STLK3	-19.5
AMPKa1	14.5	CHK2	2.4	FYN, SRC, YES	33.1	LATS1	1.0	MASTL	-2.0	p70S6K, p70S6Kb	1.7	PKR	-14.4	STLK5	-3.0
AMPKa1, AMPKa2	2.3	CHK2	-18.2	GAK	-29.6	LATS2	4.2	MASTL	6.7	p70S6Kb	-0.7	PLK1	6.1	STLK6	14.1
AMPKa1, AMPKa2	-5.2	CK1a	0.5	GCK	75.6	LATS2	-0.9	MET	13.6	PAN3	-16.8	PLK1	-8.0	STLK6	6.8
ANPb	-19.5	CK1d, CK1e	-13.4	GCK	71.1	LKB1	-7.9	MLK3	32.0	PCTAIRE1	5.9	PRP4	-8.3	TAK1	62.2
ARAF	-21.7	CK1g1	-10.2	GCN2	-2.6	LOK	-9.2	MPSK1	-19.2	PCTAIRE1, PCTAIRE3	26.2	PRP4	2.5	TAO1, TAO3	2.5
ATR	2.9	CK1g2	-2.7	GCN2	-8.9	LYN	50.6	MPSK1	-28.6	PCTAIRE2	26.8	PRPK	-10.1	TAO2	12.7
AurA	54.4	CK2a1	0.2	GPRK5	3.5	LYN	62.9	MSK1 domain1	-13.3	PCTAIRE2, PCTAIRE3	29.2	RAF1	16.6	TBK1	0.2
AurA	52.3	CK2a2	-23.4	GSK3A	-4.7	MAP2K1	1.8	MSK2 domain1	14.2	PEK	0.6	ROCK1	-18.7	TGFbR2	-14.5
AurA, AurB, AurC	64.8	CLK1	-8.1	GSK3B	1.3	MAP2K1, MAP2K2	-0.6	MST1	36.1	PFTAIRE1	47.8	ROCK1, ROCK2	7.2	TLK1	3.4
AurB	81.1	CLK2	2.2	HER2/ ErbB2	-4.5	MAP2K1, MAP2K2	-12.9	MST1, MST2	24.6	PFTAIRE1	39.4	RSK1 domain1	32.6	TLK1	-4.7
BARK1	-10.3	CLK3	4.1	HER2/ ErbB2	-15.6	MAP2K3	2.5	MST2	44.8	PHKg2	-5.7	RSK1 domain1	15.9	TLK2	-6.7
BRAF	-12.8	CRK7	6.1	HER3/ ErbB3	-5.7	MAP2K3	-3.0	MST3	36.1	PI4K2B	-11.6	RSK1/ RSK2/ RSK3 domain1	3.6	TLK2	-13.1
CaMK1a	-8.2	CSK	-2.3	HER3/ ErbB3	-24.6	MAP2K4	4.5	MST3	26.3	PI4KA, PI4KAP2	-13.6	RSK1 domain2	-4.6	ULK1	-6.3
CaMK1a	-14.4	CSK	-5.0	HSER	-8.9	MAP2K4	-13.9	MST4	-11.5	PI4KB	4.7	RSK2 domain1	11.1	ULK3	-6.7
CaMK2a, CaMK2b, CaMK2d, CaMK2g	-0.3	DNAPK	8.2	IKKa	8.5	MAP2K5	32.9	MST4, YSK1	38.8	PI4KB	-20.5	RSK2 domain1	-7.1	ULK3	2.3
CaMK2d	-7.1	DNAPK	-15.1	IKKb	-9.1	MAP2K5	33.0	NDR1	0.1	PIK3C3	-23.4	RSK2 domain1	12.4	VRK2	-24.8
CaMK2g	-3.6	eEF2K	6.4	IKKb	-22.7	MAP2K6	2.3	NDR1	-9.0	PIK3CB	-1.4	RSK2 domain1	6.4	Wnk1, Wnk2, Wnk3	2.0
CaMKK2	-15.3	EGFR	-2.3	IKKe, TBK1	22.2	MAP2K6	-9.0	NDR2	10.5	PIP4K2A	-10.1	RSK2 domain2	-10.1	Wnk1, Wnk2, Wnk4	-11.5
CASK	-19.5	EGFR	-0.3	ILK	-5.5	MAP2K7	3.7	NDR2	1.5	PIP4K2C	2.9	RSKL1	-18.5	Wnk4	14.6
CDC2	-8.1	EphA2	85.2	ILK	-2.2	MAP3K1	42.0	NEK1	-10.3	PIP4K2C	-1.5	SGK	0.9	YANK3	5.8
CDC2	-0.4	EphA2	89.3	IRAK1	14.9	MAP3K2	31.4	NEK3	-6.2	PIP5K3	-18.3	SGK3	-19.5	YES	50.8
CDK10	2.3	EphB4	81.8	IRAK4	8.3	MAP3K2, MAP3K3	10.2	NEK4	4.9	PITSLRE	-11.2	SGK3	-8.3	ZAK	20.4
CDK11, CDK8	22.4	Erk1	-1.9	IRAK4	17.3	MAP3K4	1.3	NEK6, NEK7	0.7	PKCa, PKCb	10.7	SLK	16.9	ZC1/HGK	2.0
CDK2	1.1	Erk2	1.1	IRE1	-3.2	MAPKAPK3	12.3	NEK7	18.3	PKCi	-8.6	SLK	3.0	ZC1/HGK, ZC2/TNIK, ZC3/MINK	6.8

CDK2	5.8	Erk3	0.9	JAK1	-16.2	MARK1, MARK2	-6.1	NEK9	12.5	PKCi	-16.4	SMG1	-7.8	ZC2/TNIK	6.1
CDK5	8.4	Erk5	6.6	JAK1 domain2	19.8	MARK2	-14.3	NEK9	12.7	PKD1	-0.2	SMG1	-5.3		
CDK5	-11.3	FAK	88.2	JAK1 domain2	29.7	MARK2, MARK3	-2.2	NuaK1	-2.3	PKD1, PKD2	-1.8	SNRK	-8.2		
CDK6	8.8	FER	46.2	JNK1, JNK2, JNK3	26.6	MARK3	0.8	NuaK1	13.2	PKD2	-13.4	SNRK	-12.7		
CDK7	14.3	FER	30.9	KHS1	81.4	MARK3, MARK4	-0.3	OSR1	-17.3	PKD3	-10.4	SRC	4.9		
CDK7	-13.3	FES	1.1	KHS2	69.4	MARK4	-5.8	p38a	11.7	PKD3	1.5	SRC	8.2		

**Supplemental Table 2: Kinativ mass spectroscopy profiling on HUH7 lysates with AD80.**

Percent inhibition of ATP-biotin probe labeling on kinase active site lysines measured at 1  $\mu$ M compound, quantified by targeted mass spectrometry. Kinases with multiple entries possess more than one active site lysine that can be probe labeled and detected. Experiments were completed in duplicated and performed at ActivX ([www.kinativ.com](http://www.kinativ.com)).

	APS 5-86-1	APS 5-86-2	APS 6-60-1	APS 6-60-2	APS 6-60-3	AD58	AD80	Sorafe- nib
ABL2 (Arg)	76	78	32	48	26	77	56	9
AURKA (Aurora A)	83	82	75	67	73	99	76	6
AURKB (Aurora B)	88	89	64	59	41	103	87	38
AURKC (Aurora C)	59	64	68	26	43	93	58	9
EPHA2	98	98	86	87	11	33	94	21
EPHB4	98	99	80	97	3	34	88	5
FRK (PTK5)	99	100	79	98	24	89	90	19
LYN A	95	97	75	95	40	101	88	28
MAP4K2 (GCK)	81	84	28	72	-3	61	69	0
MAP4K5 (KHS1)	104	103	94	95	61	103	103	38
MAPK11 (p38 beta)	21	29	18	32	12	13	12	-4
MAPK12 (p38 gamma)	87	89	36	36	3	20	80	6
MAPK13 (p38 delta)	66	71	41	45	5	13	12	-4
MAPK14 (p38 alpha) Direct	16	13	9	19	4	-8	-1	46
MAPK14 (p38 alpha)	11	9	5	11	15	14	2	11
PTK2 (FAK)	95	93	29	25	7	67	87	10
YES1	94	95	51	89	37	99	77	4
CDK14 (PFTK1)/ cyclin Y	100	100	97	102	37			78

**Supplemental Table 3: Percent inhibition measured in cell-free assays using recombinant, purified kinases.** Assays were conducted using 1  $\mu$ M compound and completed in duplicate. Inhibition values are normalized to DMSO controls.