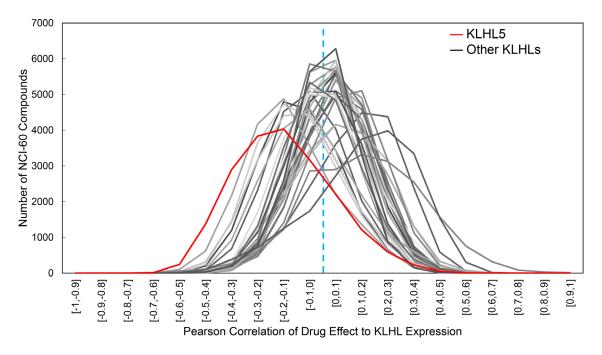
KLHL5 knockdown increases cellular sensitivity to anticancer drugs

SUPPLEMENTARY MATERIALS

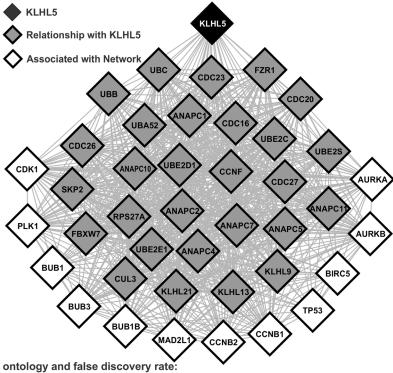


Supplementary Figure 1: Pearson correlations between KLHLs and anticancer compounds. Histogram for KLHLs indicates that KLHL5 possesses a high number of moderate or high negative correlations with compounds (< –0.4) and a distribution of correlations with the \sim 20,000 compounds that is shifted in distribution towards a negative correlation.

Mechanism Apontosis	Drug Target Bcl-2	Drug Name Navitoclax		[µM]	Obs.¬	Expecte
Apoptosis Cell Cycle	DCI-Z	Navitociax	O S	0.1		
	Aurora Kinase	AMG 900	0	0.1		_ I
	Aurora Kiriase	AIVIG 900	S	0.1	= -	
		Barasertib	0	0.1	= +	
		CYC116	0	1	=-	
		Danusertib	0	1		
		ENMD-2076	0	1		1
		PF-03814735	S	0.1	<u> </u>	
		SNS-314 Mesylate	0	0.1	=+	
		ONO-514 Mesylate	O	1	= +	
		Tozasertib	0	0.1		
	CDK	SNS-032	0	0.1		1
	Chk	AZD7762	S	0.01		•
Cytoskeletal	HSP	Ganetespib	S	0.01	$=$ \top	1
Signaling	1101	Geldanamycin	S	0.01		
DNA Damage	DNA/RNA	Fludarabine Phosphate	0	0.1		- '
	Synthesis	Nelarabine	0	0.1		
	Topoisomerase	Daunorubicin HCI	S	0.01		
	Topoisomerase	Idarubicin HCI	0	0.1		-
		Teniposide	S	0.1	= '	
Endocrinology	ER/PR	Raloxifene HCl	0	0.1		
Epigenetics	EGFR	CUDC-101	0	0.1		- I
Lpigerietics	HDAC	Entinostat	0	1	'	
	TIDAO	PCI-24781	S	0.1		
	Sirtuin	SRT1720	0	1		1 1
MAPK	MEK	TAK-733	S	0.1	$=$ \top	_
	WILK	Trametinib	S	0.1		
Metabolism	ALDH1	Disulfiram	0	1		
NF-kB	E2 conjugating	BAY 11-7082	0	1		
PI3K/Akt/mTOR		Triciribine	0	0.1		
	PI3K	GDC-0941	0	0.1		1
	1 1010	000-0041	S	0.1		1
		XL147	0	0.1		1 1
		YM201636	0	0.1		<u> </u>
		ZSTK474	S	0.1		
	mTOR	AZD8055	S	0.01		
	IIIIOIX	CH5132799	S	0.01		
		Everolimus	0	1		
		INK 128	S	0.01	=-	
		Ku-0063794	0	0.01		1
Proteases	Proteasome	Ixazomib	S	0.1		1
RTK and	EGFR	Dacomitinib	0	1	<u> </u>	
Angiogenesis	LOFIX	Daoomiumo	S	0.1		
		Erlotinib HCl	0	0.1		4
		WZ4002	0	0.1		-
	FAK	PF-562271	0	1		
			J			1
DNA Damage	DHFR	Pemetrexed	0	0.1		
Metabolism	Dehydrogenase	Mycophenolate mofetil	S	0.1	_	
PI3K/Akt/mTOR		Triciribine	S	0.1		
	mTOR	BEZ235	S	0.01		
RTK and Angi	Bcr-Abl	Rebastinib	S	0.1		
				0		50% 100 %Viability

Supplementary Figure 2: Highly synergistic/antagonistic drugs with KLHL5 knockdown. Drugs with highest synergy or antagonism with KLHL5 knockdown. Cell line (CL) SN12C (S) was treated at 0.1 and 0.01 μ M concentrations and OVCAR-8 (O) was treated at 1 and 0.1 μ M concentrations. The viabilities upon treatment with compounds with the highest differences between the expected (knockdown only x drug only) and observed (knockdown and drug combined treatment) from the screening tests are shown.

Network: Associated with KLHL5

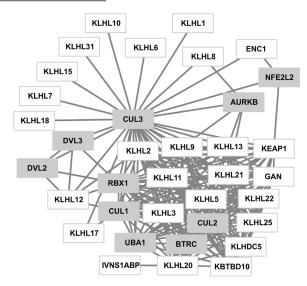


GO: 0007049 cell cycle 3.75E-30

GO: 0016567 protein ubiquitination 4.12E-42

GO: 1903047 mitotic cell cycle process 3.78E-34

Network: All KLHLs



Supplementary Figure 3: STRING network analysis. String-db.org was consulted for information about interactions between KLHLs as well as proteins known or suspected to associate with KLHL5.