SUPPLEMENTARY INFORMATION

Supplementary Table S1. DISC1 kinase network gene list.

Family	Genes
AMPK	PRKAA1; PRKAA2; PRKAB1; PRKAB2; PRKAG1; PRKAG2; PRKAG3
KHS	MAP4K1; MAP4K2; MAP4K3; MAP4K5
SGK	SGK1; SGK2; SGK3
DYRK	DYRK1A; DYRK1B; DYRK2; DYRK3; DYRK4; HIPK1; HIPK2; HIPK3; HIPK4
ERK	MAPK1; MAPK3; MAPK4; MAPK6; MAPK7
WNK	WNK1; WNK2; WNK3; WNK4
TAO	TAOK1; TAOK2; TAOK3
CAMK1	CAMK1; CAMK1D; CAMK1G; CAMK4; PNCK
MARK	MARK1; MARK2; MARK3; MARK4
MAPKAPK	MAPKAPK2; MAPKAPK3; MAPKAPK5; MKNK1; MKNK2
BUD32	TP53RK
MOS	MOS
CHK1	CHEK1
TTK	TTK
NUAK	NUAK1; NUAK2
AKT	AKT1; AKT2; AKT3
PKCA	PRKCA
SMG1	SMG1
ATM	ATM
ATR	ATR
AUR	AURKA; AURKB
BUB	BUB1; BUB1B
CAMK2	CAMK2B
CAMKK	CAMKK1; CAMKK2
CDC7	CDC7
CDK	CDK1
COT	MAP3K8
CSK	CSK
INSR	INSR
JAKA	JAK2
JNK	MAPK8; MAPK9; MAPK10
LKB	STK11
MLK	MAP3K7; MAP3K11
MTOR	MTOR; RPTOR; RICTOR; PRR5
NMO	NLK
P38	MAPK11; MAPK12; MAPK13; MAPK14
PAKA	PAK1; PAK2; PAK3
PDK1	PDPK1
PKA	PRKACA; PRKACB; PRKACG
PLK	PLK1
RAF	RAF1; BRAF; KSR1
RET	RET
RIPK	RIPK1

Supplementary Table S1. (cont.)

Family	Genes
RSK	RPS6KA1; RPS6KA2; RPS6KA3
SRC	LCK; FYN
STE11	MAP3K1; MAP3K2; MAP3K3; MAP3K5
STE7	MAP2K1; MAP2K2; MAP2K3; MAP2K5; MAP2K6
STLK	STRADA; STRADB
SYK	ZAP70
ULK	ULK1

Legend: Red and bolded text indicates direct kinome array hit. “Family” refers to the kinase families identified in the kinome array. “Genes” refer to the members of these families that were individually searched in the transcriptome databases (Supplementary Tables S2 and S3).

Supplementary Table S2. Enrichr cell pathway analysis (KEGG 2016) of the DISC1 kinase network.

Pathway	p-value	Associated kinases
MAPK signaling pathway	1.78E-59	RPS6KA3; AKT2; PRKACG; RPS6KA2; AKT3; RPS6KA1; AKT1; MAP3K8; PRKACA; PRKACB; MAP3K7; MAP3K5; MAP4K1; MAP2K3; MAP4K2; MAP2K1; MAP2K2; PRKCA; MAPKAPK3; MAPKAPK2; MAPKAPK5; RAF1; NLK; MAPK9; PAK1; MAPK8; MAPK7; MKNK1; MKNK2; MAPK1; PAK2; MAP4K3; MAP2K5; MAP2K6; MAPK3; MAP3K2; MAP3K3; MAP3K1; BRAF; MAPK14; MAPK12; MAPK13; MAPK10; MOS; MAPK11; TAOK3; TAOK1; TAOK2; MAP3K11
FoxO signaling pathway	3.42E-41	PRKAA1; PRKAA2; PRKAG1; PRKAG2; NLK; PRKAG3; MAPK9; STK11; MAPK8; AKT2; AKT3; AKT1; MAPK1; MAPK3; PRKAB2; MAP2K1; MAP2K2; PDPK1; INSR; PLK1; BRAF; MAPK14; PRKAB1; MAPK12; MAPK13; MAPK10; MAPK11; ATM; SGK3; RAF1; SGK1; SGK2
Neurotrophin signaling pathway	1.56E-35	CAMK2B; MAPK9; RPS6KA3; MAPK8; MAPK7; AKT2; RPS6KA2; AKT3; RPS6KA1; AKT1; MAPK1; MAP2K5; MAP3K5; MAPK3; MAP3K3; MAP2K1; MAP3K1; MAP2K2; PDPK1; BRAF; MAPK14; MAPK12; MAPK13; MAPK10; MAPK11; CAMK4; MAPKAPK2; RAF1
Insulin signaling pathway	1.09E-33	PRKAA1; PRKAA2; PRKAG1; PRKAG2; PRKAG3; RPTOR; MAPK9; MAPK8; AKT2; PRKACG; MKNK1; AKT3; MKNK2; AKT1; MAPK1; PRKACA; PRKACB; MAPK3; PRKAB2; MAP2K1; MAP2K2; PDPK1; INSR; BRAF; PRKAB1; MTOR; MAPK10; RAF1
mTOR signaling pathway	4.12E-27	PRKAA1; PRKAA2; STRADA; PDPK1; BRAF; PRKCA; MTOR; RPTOR; RPS6KA3; STK11; AKT2; RPS6KA2; AKT3; RPS6KA1; AKT1; MAPK1; ULK1; RICTOR; MAPK3
AMPK signaling pathway	8.82E-24	PRKAB2; PRKAA1; PRKAA2; STRADA; PDPK1; INSR; STRADB; PRKAG1; PRKAG2; PRKAB1; MTOR; PRKAG3; CAMKK1; CAMKK2; RPTOR; STK11; AKT2; AKT3; AKT1; ULK1; MAP3K7

Supplementary Table S3. Gene and protein expression changes in kinases emerging as direct kinome array hits in D2-1 vs. C3-1 cells.

		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		D2-1 vs. C3-1 Proteomics	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value
AMPK	PRKAA1	**0.325**	**0.471**	*	
	PRKAA2	-0.013	0.890	*	
	PRKAB1	-0.058	0.824	*	
	PRKAB2	**-0.328**	**0.497**	*	
	PRKAG1	-0.136	0.585	*	
	PRKAG2	**0.824**	**0.016**	*	
	PRKAG3	-	-	*	
KHS	MAP4K1	-	-	*	
	MAP4K2	**1.186**	**0.074**	*	
	MAP4K3	**-0.981**	**0.211**	*	
	MAP4K5	**-0.644**	**0.181**	**0.456**	**0.008**
SGK	SGK1	0.091	0.889	*	
	SGK2	-	-	*	
	SGK3	**1.088**	**0.037**	*	
DYRK	DYRK1A	0.191	0.636	*	
	DYRK1B	**1.530**	**0.154**	**0.497**	**0.039**
	DYRK2	0.229	0.250	*	
	DYRK3	**-0.511**	**0.046**	*	
	DYRK4	**-0.493**	**0.148**	*	
	HIPK1	-0.251	0.403	*	
	HIPK2	**-0.359**	**0.350**	*	
	HIPK3	**0.357**	**0.031**	*	
	HIPK4	-	-	*	
ERK	MAPK1	-0.189	0.636	0.232	0.059
	MAPK3	**-0.310**	**0.235**	**-0.622**	**0.024**
	MAPK4	**1.530**	**0.002**	*	
	MAPK6	-0.096	0.752	**0.689**	**0.014**
	MAPK7	**0.538**	**0.025**	*	
WNK	WNK1	**0.868**	**0.084**	*	
	WNK2	-0.050	0.947	**-0.503**	**0.001**
	WNK3	-0.116	0.652	*	
	WNK4	-	-	*	
TAO	TAOK1	**0.447**	**0.106**	**0.561**	**0.001**
	TAOK2	**0.891**	**0.085**	**0.490**	**0.010**
	TAOK3	**0.820**	**0.030**	**0.739**	**0.003**
CAMK1	CAMK1	**1.537**	**0.001**	*	
	PNCK	**1.132**	**0.086**	*	
	CAMK1D	-0.021	0.877	*	
	CAMK1G	**1.697**	**0.007**	*	
	CAMK4	**1.293**	**0.093**	**0.472**	**0.008**
MARK	MARK1	0.294	0.648	*	
	MARK2	**0.354**	**0.240**	*	
	MARK3	0.084	0.786	**0.485**	**0.011**
	MARK4	**0.590**	**0.187**	**0.641**	**0.006**
MAPKAPK	MAPKAPK2	-0.169	0.524	**-0.511**	**0.036**
	MAPKAPK3	**-0.887**	**0.003**	**-0.622**	**0.024**
	MAPKAPK5	**0.395**	**0.088**	**0.453**	**0.004**
	MKNK1	**-0.469**	**0.089**	*	
	MKNK2	0.246	0.753	*	
BUD32	TP53RK	**0.736**	**0.002**	-0.270	0.125
MOS	MOS	-	-	*	
CHK1	CHEK1	**0.384**	**0.061**	**0.432**	**0.025**
TTK	TTK	**0.556**	**0.062**	*	
NUAK	NUAK1	**-0.374**	**0.258**	0.250	0.003
	NUAK2	**-0.922**	**0.001**	*	

Legend: Red and bolded text indicates genes with log2 FC > 0.3 or log2 FC < -0.3. * no fragments identified in LC-MS/MS

Supplementary Table S4. Gene and protein expression changes in kinases emerging as indirect kinome array hits (i.e. connected via STRING with the direct kinome array hits) in D2-1 vs. C3-1 cells.

		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		D2-1 vs. C3-1 Proteomics	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value
AKT	AKT1	**0.628**	**0.090**	**0.393**	**0.094**
	AKT2	-0.076	0.591	*	
	AKT3	-0.215	0.365	*	
PKCA	PRKCA	**1.958**	**0.004**	**1.148**	**0.012**
SMG1	SMG1	0.156	0.499	**0.611**	**0.008**
ATM	ATM	**-0.680**	**0.263**	**-0.692**	**0.035**
ATR	ATR	**-0.475**	**0.138**	*	
AUR	AURKA	**0.464**	**0.034**	*	
	AURKB	**-0.971**	**0.380**	**1.010**	**0.039**
BUB	BUB1	**0.300**	**0.189**	*	
	BUB1B	0.107	0.650	*	
CAMK2	CAMK2B	**1.407**	**0.010**	**0.818**	**0.001**
CAMKK	CAMKK1	**0.586**	**0.025**	**0.498**	**0.007**
	CAMKK2	**0.562**	**0.084**	**1.100**	**0.014**
CDC7	CDC7	**1.115**	**0.030**	*	
CDK	CDK1	**0.727**	**0.119**	**0.631**	**0.003**
COT	MAP3K8	**-0.862**	**0.112**	*	
CSK	CSK	**0.869**	**0.143**	**0.548**	**0.024**
INSR	INSR	**0.309**	**0.258**	*	
JAKA	JAK2	**1.201**	**0.008**	*	
JNK	MAPK8	**0.441**	**0.154**	**0.712**	**0.008**
	MAPK9	**0.817**	**0.019**	*	
	MAPK10	-0.068	0.769	*	
LKB	STK11	0.187	0.715	*	
MLK	MAP3K11	-0.153	0.826	*	
	MAP3K7	**-0.375**	**0.172**	*	
MTOR	MTOR	**0.364**	**0.064**	*	
	RPTOR	**0.726**	**0.323**	*	
	RICTOR	**-0.375**	**0.372**	*	
	PRR5	**-0.942**	**0.016**	**-0.840**	**0.027**
NMO	NLK	**0.459**	**0.144**	*	
P38	MAPK11	0.082	0.707	*	
	MAPK12	**0.539**	**0.204**	*	
	MAPK13	**0.330**	**0.171**	*	
	MAPK14	-0.027	0.928	**-0.639**	**0.001**
PAKA	PAK1	**0.301**	**0.231**	**0.836**	**0.001**
	PAK2	**0.484**	**0.185**	**0.753**	**0.003**
	PAK3	**0.346**	**0.152**	*	
PDK1	PDPK1	0.237	0.398	*	
PKA	PRKACA	**0.392**	**0.260**	**0.653**	**0.001**
	PRKACB	**0.716**	**0.006**	*	
	PRKACG	-	-	*	
PLK	PLK1	0.069	0.883	*	
RAF	RAF1	**0.518**	**0.177**	*	
	BRAF	0.218	0.155	*	
	KSR1	0.164	0.535	*	
RET	RET	0.070	0.934	*	
RIPK	RIPK1	-0.181	0.355	**-1.291**	**0.001**
RSK	RPS6KA1	-0.014	0.972	*	
	RPS6KA2	-0.070	0.816	*	
	RPS6KA3	**-0.352**	**0.116**	**-0.344**	**0.020**
SRC	LCK	**0.744**	**0.053**	*	
	FYN	**0.548**	**0.011**	**0.492**	**0.010**
STE11	MAP3K1	**0.552**	**0.111**	*	
	MAP3K2	0.042	0.883	*	
	MAP3K3	0.229	0.524	*	
	MAP3K5	**-0.802**	**0.108**	**-1.048**	**0.015**
STE7	MAP2K1	0.218	0.218	*	
	MAP2K2	0.090	0.488	*	
	MAP2K3	**-0.309**	**0.209**	*	
	MAP2K5	**0.343**	**0.440**	*	
	MAP2K6	-	-	**0.550**	**0.029**

Supplementary Table S4. (cont.)

STLK	STRADA	-	-	*
	STRADB	-0.050	0.896	*
SYK	ZAP70	**-1.146**	**0.036**	*
ULK	ULK1	-0.060	0.787	*

Legend: Red and bolded text indicates genes with log2 FC > 0.3 or log2 FC < -0.3. * no fragments identified in LC-MS/MS

Supplementary Table S5. Gene expression changes in kinases emerging as direct kinome array hits in cell-level and region-level transcriptome databases of schizophrenia.

		CELL-LEVEL								REGION-LEVEL					
		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		Schizophrenia iPSC Microarray (Brennand et al., 2011)		Schizophrenia LCM Superficial Neurons Microarray		Schizophrenia LCM Deep Neurons Microarray		Postmortem Meta-Analysis Microarray (Gandal et al., 2018)		SMRI Genomics (Higgs et al., 2006)		Mt. Sinai Microarray (Roussos et al., 2012)	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	Probes
AMPK	PRKAA1	**0.325**	**0.471**	0.080	0.546	-0.092	0.660	**0.334**	**0.140**	-0.020	0.594	-0.003	0.878	-0.185	3
	PRKAA2	-0.013	0.890	-0.211	0.320	0.093	0.526	-0.069	0.640	-0.013	0.748	0.050	0.279	**0.303**	**1**
	PRKAB1	-0.058	0.824	-0.048	0.584	0.237	0.460	0.090	0.774	0.023	0.397	0.000	0.990	**-0.301**	**1**
	PRKAB2	**-0.328**	**0.497**	-0.068	0.599	**0.635**	**0.020**	-0.169	0.315	**0.089**	**0.013**	0.059	0.071	-0.089	2
	PRKAG1	-0.136	0.585	0.120	0.328	**0.365**	**0.150**	**0.436**	**0.111**	-0.019	0.418	0.009	0.854	0.009	1
	PRKAG2	**0.824**	**0.016**	-0.088	0.488	0.016	0.969	**-0.725**	**0.067**	-0.017	0.617	-0.015	0.504	-0.097	3
	PRKAG3	-	-	-0.003	0.983	0.023	0.847	0.138	0.336	-	-	-0.026	0.782	-	-
KHS	MAP4K1	-	-	0.036	0.850	**-0.388**	**0.071**	**0.383**	**0.098**	0.005	0.902	0.000	0.989	-	-
	MAP4K2	**1.186**	**0.074**	-0.022	0.905	-0.163	0.358	**-0.390**	**0.030**	**-0.052**	**0.019**	0.007	0.808	-	-
	MAP4K3	**-0.981**	**0.211**	0.100	0.243	**0.660**	**0.155**	-0.245	0.604	-0.010	0.858	-0.007	0.903	-0.156	1
	MAP4K5	**-0.644**	**0.181**	0.044	0.716	0.067	0.865	-0.085	0.790	0.050	0.453	0.014	0.597	-0.207	3
SGK	SGK1	0.091	0.889	**0.928**	**0.021**	**0.452**	**0.404**	**0.952**	**0.051**	0.169	0.058	0.180	0.075	**-0.515**	**1**
	SGK2	-	-	**-0.353**	**0.024**	0.046	0.691	-0.003	0.984	0.029	0.651	0.015	0.510	-	-
	SGK3	**1.088**	**0.037**	-0.122	0.418	0.124	0.635	-0.158	0.343	-	-	**0.143**	**0.003**	0.050	2
DYRK	DYRK1A	0.191	0.636	0.114	0.315	-0.266	0.411	-0.122	0.751	0.006	0.836	-0.003	0.897	-0.096	1
	DYRK1B	**1.530**	**0.154**	-0.092	0.409	0.247	0.133	-0.049	0.783	-0.005	0.890	0.022	0.652	-	-
	DYRK2	0.229	0.250	0.023	0.909	0.108	0.328	0.142	0.260	0.001	0.984	0.020	0.345	0.228	2
	DYRK3	**-0.511**	**0.046**	-0.130	0.324	0.056	0.828	-0.290	0.183	0.024	0.422	-0.011	0.603	-	-
	DYRK4	**-0.493**	**0.148**	-0.168	0.197	-0.111	0.635	-0.176	0.462	0.009	0.728	-0.010	0.805	0.028	-
	HIPK1	-0.251	0.403	-0.231	0.279	-0.166	0.332	0.269	0.159	0.038	0.213	0.025	0.536	-0.031	2
	HIPK2	**-0.359**	**0.350**	-0.243	0.151	**0.442**	**0.040**	0.153	0.553	0.075	0.130	0.033	0.158	0.072	6
	HIPK3	**0.357**	**0.031**	0.019	0.919	0.241	0.133	-0.008	0.945	0.037	0.135	-0.009	0.588	**-0.325**	**2**
	HIPK4	-	-	-0.069	0.489	**-0.303**	**0.140**	**-0.673**	**0.011**	-	-	-	-	-	-
ERK	MAPK1	-0.189	0.636	-0.059	0.788	0.273	0.093	0.249	0.086	-0.001	0.980	-0.063	0.076	0.002	3
	MAPK3	**-0.310**	**0.235**	-0.025	0.880	0.222	0.480	0.047	0.841	0.041	0.086	-0.008	0.872	-0.002	1
	MAPK4	**1.530**	**0.002**	**-0.595**	**0.073**	-0.103	0.596	-0.131	0.406	0.019	0.661	0.016	0.513	-	-
	MAPK6	-0.096	0.752	**0.363**	**0.011**	0.158	0.406	-0.062	0.709	**-0.074**	**0.002**	-0.065	0.279	0.017	1
	MAPK7	**0.538**	**0.025**	-0.006	0.966	-0.054	0.727	0.068	0.562	0.026	0.320	0.007	0.788	-	-
WNK	WNK1	**0.868**	**0.084**	0.281	0.091	**0.473**	**0.271**	**0.806**	**0.016**	0.059	0.056	**0.073**	**0.003**	0.134	3
	WNK2	-0.050	0.947	**0.247**	**0.043**	-0.044	0.856	0.260	0.166	-	-	0.008	0.818	0.022	1
	WNK3	-0.116	0.652	-0.106	0.651	0.019	0.892	-0.066	0.523	-	-	-0.011	0.716	-0.111	1
	WNK4	-	-	-0.106	0.332	**-0.354**	**0.058**	-0.242	0.135	-	-	0.016	0.776	-	-
TAO	TAOK1	**0.447**	**0.106**	0.145	0.336	0.279	0.204	-0.160	0.473	**0.039**	**0.029**	0.012	0.881	0.173	1
	TAOK2	**0.891**	**0.085**	-0.042	0.589	-0.136	0.560	-0.258	0.362	-0.027	0.255	0.015	0.516	-0.182	1
	TAOK3	**0.820**	**0.030**	-0.054	0.873	**0.468**	**0.248**	**0.573**	**0.117**	-0.028	0.312	0.001	0.966	0.213	2

Supplementary Table S5. (cont.)

		CELL-LEVEL								REGION-LEVEL					
		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		Schizophrenia iPSC Microarray (Brennand et al., 2011)		Schizophrenia LCM Superficial Neurons Microarray		Schizophrenia LCM Deep Neurons Microarray		Postmortem Meta-Analysis Microarray (Gandal et al., 2018)		SMRI Genomics (Higgs et al., 2006)		Mt. Sinai Microarray (Roussos et al., 2012)	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	Probes
CAMK1	CAMK1	**1.537**	**0.001**	-0.160	0.061	**0.321**	**0.331**	**0.366**	**0.210**	**-0.096**	**0.001**	-0.060	0.226	0.026	1
	PNCK	**1.132**	**0.086**	**-0.160**	**0.034**	0.151	0.383	-0.163	0.223	-	-	-0.014	0.808	0.120	1
	CAMK1D	-0.021	0.877	**0.765**	**0.001**	0.132	0.386	-0.102	0.445	-0.038	0.150	0.052	0.141	0.009	2
	CAMK1G	**1.697**	**0.007**	0.169	0.145	**0.553**	**0.002**	0.089	0.570	0.025	0.650	-0.026	0.510	-0.142	2
	CAMK4	**1.293**	**0.093**	**0.507**	**0.110**	-0.280	0.197	-0.300	0.052	-0.057	0.094	-0.034	0.221	0.184	1
MARK	MARK1	0.294	0.648	0.242	0.271	0.037	0.890	**0.316**	**0.159**	**-0.064**	**0.044**	-0.029	0.160	-0.016	2
	MARK2	**0.354**	**0.240**	0.107	0.329	0.012	0.897	-0.171	0.051	**-0.068**	**0.023**	0.030	0.129	-	-
	MARK3	0.084	0.786	-0.007	0.968	0.294	0.239	**-0.473**	**0.035**	-0.005	0.839	-0.011	0.706	-0.076	3
	MARK4	**0.590**	**0.187**	-0.028	0.786	0.263	0.110	0.204	0.255	-0.029	0.226	-0.021	0.611	-0.043	1
MAPKAPK	MAPKAPK2	-0.169	0.524	-0.072	0.305	0.123	0.281	-0.010	0.937	0.019	0.545	0.027	0.224	0.077	2
	MAPKAPK3	**-0.887**	**0.003**	0.050	0.755	-0.133	0.354	0.062	0.582	**0.063**	**0.035**	0.034	0.259	**0.305**	**1**
	MAPKAPK5	**0.395**	**0.088**	0.104	0.293	0.224	0.071	-0.031	0.831	**-0.077**	**0.003**	-0.008	0.803	0.160	1
	MKNK1	**-0.469**	**0.089**	0.058	0.723	-0.142	0.208	-0.048	0.678	**0.069**	**0.001**	0.081	0.120	0.026	2
	MKNK2	0.246	0.753	**0.380**	**0.001**	0.110	0.615	-0.127	0.570	0.041	0.299	-0.022	0.423	**0.631**	**2**
BUD32	TP53RK	**0.736**	**0.002**	0.058	0.540	-0.216	0.281	0.038	0.844	-	-	-0.049	0.348	-	-
MOS	MOS	-	-	0.004	0.983	0.107	0.346	-0.074	0.665	-0.016	0.617	-0.005	0.904	-	-
CHK1	CHEK1	**0.384**	**0.061**	-0.106	0.354	0.265	0.173	0.068	0.758	0.005	0.885	0.008	0.606	0.292	1
TTK	TTK	**0.556**	**0.062**	0.122	0.663	0.113	0.433	**-0.337**	**0.029**	**0.043**	**0.009**	0.034	0.107	-	-
NUAK	NUAK1	**-0.374**	**0.258**	0.094	0.750	0.267	0.079	-0.018	0.914	**-0.093**	**0.002**	-0.073	0.375	-0.097	1
	NUAK2	**-0.922**	**0.001**	-0.006	0.975	-0.005	0.969	-0.089	0.477	0.023	0.466	0.019	0.632	0.149	1

Legend: Red and bolded text indicates genes with log2 FC > 0.3, log2 FC < -0.3, as well as significant findings (p < 0.05) irrespective of FC values

Supplementary Table S6. Gene expression changes in kinases emerging as indirect kinome array hits (i.e. connected via STRING with the direct kinome array hits) in cell-level and region-level transcriptome databases of schizophrenia.

		CELL-LEVEL								REGION-LEVEL					
		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		Schizophrenia iPSC Microarray (Brennand et al., 2011)		Schizophrenia LCM Superficial Neurons Microarray		Schizophrenia LCM Deep Neurons Microarray		Postmortem Meta-Analysis Microarray (Gandal et al., 2018)		SMRI Genomics (Higgs et al., 2006)		Mt. Sinai Microarray (Roussos et al., 2012)	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	Probes
AKT	AKT1	**0.628**	**0.090**	-0.062	0.388	-0.030	0.857	0.131	0.506	-0.018	0.418	-0.036	0.549	0.135	1
	AKT2	-0.076	0.591	-0.194	0.071	**0.752**	**0.009**	**0.460**	**0.151**	0.007	0.850	-0.011	0.344	-	-
	AKT3	-0.215	0.365	-0.088	0.745	**0.461**	**0.539**	-0.160	0.802	-0.022	0.448	-0.021	0.554	0.018	5
PKCA	PRKCA	**1.958**	**0.004**	**-1.269**	**0.000**	-0.139	0.674	0.034	0.904	0.025	0.383	0.018	0.304	-0.218	1
SMG1	SMG1	0.156	0.499	0.060	0.534	**-0.755**	**0.242**	0.058	0.906	**0.077**	**0.001**	0.026	0.178	0.046	4
ATM	ATM	**-0.680**	**0.263**	0.104	0.392	-0.263	0.286	0.081	0.705	0.024	0.672	0.043	0.230	-0.104	3
ATR	ATR	**-0.475**	**0.138**	0.087	0.599	**-0.512**	**0.116**	**-0.446**	**0.228**	-0.039	0.227	-0.003	0.942	-0.118	2
AUR	AURKA	**0.464**	**0.034**	-0.047	0.885	0.039	0.867	-0.277	0.340	-0.054	0.051	-0.027	0.316	-	-
	AURKB	**-0.971**	**0.380**	-0.142	0.327	-0.005	0.978	0.192	0.377	0.006	0.849	-0.006	0.879	-	-
BUB	BUB1	**0.300**	**0.189**	-0.063	0.760	0.100	0.642	**0.397**	**0.039**	0.027	0.434	0.006	0.766	-	-
	BUB1B	0.107	0.650	-0.150	0.471	-0.100	0.535	0.244	0.086	-0.021	0.435	-0.019	0.526	-	-
CAMK2	CAMK2B	**1.407**	**0.010**	**0.395**	**0.171**	0.066	0.877	**0.368**	**0.467**	**-0.080**	**0.004**	-0.033	0.273	0.067	5
CAMKK	CAMKK1	**0.586**	**0.025**	-0.125	0.343	0.250	0.129	0.018	0.907	-	-	0.019	0.811	-	-
	CAMKK2	**0.562**	**0.084**	0.185	0.138	**-0.570**	**0.069**	**-0.466**	**0.082**	**-0.190**	**0.001**	-0.009	0.830	-0.008	3
CDC7	CDC7	**1.115**	**0.030**	-0.184	0.187	0.100	0.455	0.070	0.714	-0.053	0.282	-0.048	0.321	-0.028	1
CDK	CDK1	**0.727**	**0.119**	-0.025	0.930	0.042	0.826	-0.087	0.745	**-0.047**	**0.023**	0.021	0.226	-	-
COT	MAP3K8	**-0.862**	**0.112**	0.205	0.199	-0.050	0.843	-0.203	0.458	0.016	0.577	0.016	0.490	-	-
CSK	CSK	**0.869**	**0.143**	0.115	0.181	-0.130	0.447	**-0.441**	**0.006**	-0.021	0.340	-0.043	0.327	**0.609**	**1**
INSR	INSR	**0.309**	**0.258**	-0.102	0.168	-0.010	0.923	-0.082	0.559	-0.011	0.745	0.025	0.431	-0.027	1
JAKA	JAK2	**1.201**	**0.008**	0.214	0.189	-0.040	0.848	**-0.756**	**0.009**	**0.066**	**0.048**	0.027	0.242	**-0.420**	**2**
JNK	MAPK8	**0.441**	**0.154**	**0.506**	**0.007**	**0.404**	**0.249**	-0.031	0.870	-0.031	0.296	-0.029	0.251	0.145	3
	MAPK9	**0.817**	**0.019**	0.246	0.109	**0.602**	**0.029**	-0.289	0.166	**-0.086**	**0.007**	-0.088	0.059	-0.114	3
	MAPK10	-0.068	0.769	-0.063	0.877	**0.342**	**0.204**	0.097	0.680	-0.019	0.563	-0.010	0.835	-0.170	1
LKB	STK11	0.187	0.715	-0.080	0.489	0.161	0.381	-0.033	0.826	-0.009	0.702	-0.017	0.611	0.096	2
MLK	MAP3K11	-0.153	0.826	-0.059	0.673	-0.284	0.173	**0.305**	**0.242**	-0.018	0.633	-0.024	0.560	0.144	1
	MAP3K7	**-0.375**	**0.172**	0.106	0.233	0.137	0.506	0.211	0.340	0.020	0.535	0.026	0.238	-0.044	2
MTOR	MTOR	**0.364**	**0.064**	0.029	0.748	0.095	0.299	-0.014	0.862	-0.004	0.883	-0.007	0.787	0.002	1
	RPTOR	**0.726**	**0.323**	-0.120	0.112	-0.284	0.245	-0.174	0.402	-	-	-0.046	0.432	-	-
	RICTOR	**-0.375**	**0.372**	0.222	0.145	0.292	0.122	-0.081	0.534	-	-	0.056	0.094	-0.295	3
	PRR5	**-0.942**	**0.016**	**0.207**	**0.013**	-0.114	0.509	-0.109	0.575	0.013	0.685	0.034	0.142	-0.059	1
NMO	NLK	**0.459**	**0.144**	**-0.342**	**0.158**	**0.460**	**0.090**	0.139	0.513	-0.028	0.437	0.076	0.074	-0.152	3
P38	MAPK11	0.082	0.707	-0.141	0.200	-0.066	0.663	0.080	0.637	-0.025	0.384	-0.008	0.636	0.025	1
	MAPK12	**0.539**	**0.204**	-0.130	0.123	-0.172	0.123	0.080	0.531	-0.022	0.582	-0.010	0.373	0.210	1
	MAPK13	**0.330**	**0.171**	-0.074	0.529	0.128	0.524	0.008	0.959	-0.029	0.374	-0.015	0.687	-0.032	1
	MAPK14	-0.027	0.928	0.043	0.665	0.164	0.424	0.011	0.951	0.021	0.439	0.005	0.789	0.009	2

Supplementary Table S6. (cont.)

		CELL-LEVEL								REGION-LEVEL					
		D2-1 vs. C3-1 RNA-Seq (Wen et al., 2014)		Schizophrenia iPSC Microarray (Brennand et al., 2011)		Schizophrenia LCM Superficial Neurons Microarray		Schizophrenia LCM Deep Neurons Microarray		Postmortem Meta-Analysis Microarray (Gandal et al., 2018)		SMRI Genomics (Higgs et al., 2006)		Mt. Sinai Microarray (Roussos et al., 2012)	
Family	Gene	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	P-value	Log2 FC	Probes
PAKA	PAK1	**0.301**	**0.231**	**0.610**	**0.005**	**0.450**	**0.134**	-0.193	0.550	-0.064	0.136	-0.077	0.090	**-0.368**	**2**
	PAK2	**0.484**	**0.185**	0.241	0.107	-0.112	0.606	-0.152	0.403	**0.069**	**0.028**	0.002	0.877	0.037	4
	PAK3	**0.346**	**0.152**	**0.321**	**0.447**	**0.730**	**0.302**	**0.341**	**0.577**	-0.028	0.357	0.006	0.822	0.005	1
PDK1	PDPK1	0.237	0.398	**0.016**	**0.010**	0.101	0.542	0.043	0.783	-0.002	0.964	0.006	0.760	0.210	3
PKA	PRKACA	**0.392**	**0.260**	0.162	0.082	**-0.381**	**0.341**	**0.705**	**0.276**	-0.020	0.376	0.019	0.328	-0.094	1
	PRKACB	**0.716**	**0.006**	0.091	0.657	**0.422**	**0.135**	-0.228	0.508	-0.039	0.123	-0.084	0.144	-0.134	3
	PRKACG	-	-	-0.010	0.955	-0.166	0.280	0.235	0.214	-0.015	0.583	0.047	0.434	-	-
PLK	PLK1	0.069	0.883	0.110	0.668	-0.277	0.465	-0.072	0.883	0.027	0.279	-0.028	0.765	-	-
RAF	RAF1	**0.518**	**0.177**	0.095	0.360	-0.074	0.630	-0.020	0.880	-0.008	0.784	-0.007	0.700	0.130	1
	BRAF	0.218	0.155	0.088	0.499	0.226	0.143	0.136	0.379	-0.024	0.201	-0.001	0.953	-0.127	2
	KSR1	0.164	0.535	0.033	0.826	0.208	0.298	0.116	0.554	0.021	0.426	0.027	0.108	-0.089	1
RET	RET	0.070	0.934	-0.069	0.480	-0.268	0.083	-0.073	0.782	-0.013	0.737	-0.044	0.098	**-0.420**	**1**
RIPK	RIPK1	-0.181	0.355	-0.023	0.873	-0.183	0.106	0.143	0.317	0.046	0.084	0.064	0.098	0.055	1
RSK	RPS6KA1	-0.014	0.972	-0.026	0.884	0.093	0.859	-0.016	0.975	0.015	0.654	0.032	0.451	0.062	1
	RPS6KA2	-0.070	0.816	-0.083	0.601	0.174	0.447	0.261	0.308	**0.059**	**0.021**	-0.004	0.925	-0.064	2
	RPS6KA3	**-0.352**	**0.116**	0.099	0.526	0.189	0.615	0.213	0.342	**-0.095**	**0.004**	**-0.096**	**0.013**	-0.097	2
SRC	LCK	**0.744**	**0.053**	0.013	0.927	0.178	0.401	**0.420**	**0.115**	0.014	0.651	0.026	0.316	-	-
	FYN	**0.548**	**0.011**	0.068	0.728	0.217	0.427	0.261	0.460	0.032	0.092	**0.055**	**0.040**	-0.019	3
STE11	MAP3K1	**0.552**	**0.111**	-0.180	0.265	0.083	0.515	-0.118	0.470	-0.049	0.157	0.014	0.540	0.149	1
	MAP3K2	0.042	0.883	0.194	0.050	0.221	0.081	-0.218	0.086	**0.054**	**0.038**	0.020	0.306	-0.148	2
	MAP3K3	0.229	0.524	0.043	0.757	-0.232	0.359	-0.266	0.101	0.006	0.841	0.007	0.674	0.167	2
	MAP3K5	**-0.802**	**0.108**	-0.209	0.323	-0.036	0.812	-0.007	0.951	0.039	0.130	0.014	0.669	0.069	2
STE7	MAP2K1	0.218	0.218	-0.047	0.740	**0.399**	**0.012**	-0.142	0.347	-0.008	0.870	-0.093	0.202	-0.033	1
	MAP2K2	0.090	0.488	-0.020	0.902	-0.246	0.480	**0.465**	**0.224**	-0.032	0.172	-0.003	0.892	0.130	2
	MAP2K3	**-0.309**	**0.209**	0.030	0.800	-0.075	0.566	**0.301**	**0.095**	-0.030	0.283	0.048	0.070	-0.085	2
	MAP2K5	**0.343**	**0.440**	0.107	0.220	0.095	0.657	0.036	0.831	-0.024	0.411	-0.024	0.209	-0.020	1
	MAP2K6	-	-	**0.361**	**0.072**	0.067	0.791	0.162	0.498	0.041	0.055	0.005	0.798	-0.064	1
STLK	STRADA	-	-	-0.054	0.611	0.195	0.252	0.108	0.562	-0.005	0.826	0.009	0.749	-0.158	1
	STRADB	-0.050	0.896	-0.085	0.610	**-0.525**	**0.008**	-0.024	0.858	-	-	0.113	0.420	-0.048	1
SYK	ZAP70	**-1.146**	**0.036**	0.079	0.606	-0.005	0.967	-0.187	0.252	0.010	0.768	0.033	0.344	-	-
ULK	ULK1	-0.060	0.787	0.100	0.238	**0.442**	**0.013**	0.013	0.943	-0.003	0.943	-0.003	0.951	0.131	1

Legend: Red and bolded text indicates genes with log2 FC > 0.3, log2 FC < -0.3, as well as significant findings ($p < 0.05$) irrespective of FC values

Supplementary Table S7. iLINCS seed gene profile.

Gene	Log2 FC D2-1 vs. C3-1 *
ATM	-0.680
ATR	-0.475
AURKB	-0.971
DYRK3	-0.511
DYRK4	-0.493
HIPK2	-0.359
MAP2K3	-0.309
MAP3K5	-0.802
MAP3K7	-0.375
MAP4K3	-0.981
MAP4K5	-0.644
MAPK3	-0.310
MAPKAPK3	-0.887
MKNK1	-0.469
NUAK1	-0.374
NUAK2	-0.922
PRKAB2	-0.328
RICTOR	-0.375
RPS6KA3	-0.352
ZAP70	-1.146

* RNA-Seq (Wen et al., 2014)

Supplementary Table S8. iLINCS clustering analysis: panel of upregulated genes.

Gene	Average LogFC *
ADRB2	0.401820605
ATF5	0.169859105
BAMBI	0.2695171
CHP1	0.416188885
DENND2D	0.43825852
DUSP4	0.392977373
E2F2	0.250831536
EML3	0.321514175
ERBB3	0.366640831
FAM63A	0.363990073
FBXO11	0.60392196
FOXO4	0.298186648
GATA3	0.448330085
GHR	0.44065004
GPATCH8	0.330894715
HES1	0.42321037
HMOX1	0.417071058
IGHMBP2	0.265536039
LGMN	0.40424956
MAMLD1	0.888830034
MBNL2	0.249295194
MCOLN1	0.721311094
MOK	0.118908403
NFKBIB	0.271989135
PAK1	0.5012496
PIK3C2B	-0.06246492
RAB11FIP2	0.35186639
RASA1	0.488406755
RRS1	0.50411191
SATB1	0.592353195
SLC1A4	0.520457751
SLC25A4	-0.05051597
SMAD3	0.3742494
SQRDL	0.34348778
ST3GAL5	0.5865712
ST6GALNAC2	0.297048045
STAP2	0.319465505
TGFBR2	0.643680175
TIMM22	0.247726675
TRAM2	0.214329109

* Average across all 20 knockdown seed gene signatures.

Supplementary Table S9. iLINCS clustering analysis: panel of downregulated genes.

Gene	Average LogFC *
ALDH7A1	-0.360678625
AURKA	-0.135923765
BIRC5	-0.220188925
BPHL	-0.505231895
C2CD5	-0.408194685
CANT1	-0.498588105
CCNB2	-0.25161366
CCNE2	-0.250046635
CDC45	-0.46445862
CDK1	-0.35988596
CENPE	-0.16989526
CHIC2	-0.343102685
CNPY3	-0.4935864
CREB1	-0.310554325
DLD	-0.36031447
DNAJA3	-0.572695645
DSG2	-0.222115365
GNAS	-0.495004465
GTPBP8	-0.542544715
HAT1	-0.257890995
HIST1H2BK	-0.421755145
HMG20B	-0.307934895
ITGAE	-0.49588866
LSM5	-0.302891705
MRPS16	-0.61689706
NR2F6	-0.78559704
NUSAP1	-0.530941
PCNA	-0.518339065
POLR2I	-0.365507561
PWP1	-0.29947801
RAD51C	-0.083694785
RNF167	-0.51768323
STMN1	-0.301101946
TM9SF3	-0.345913077
TOR1A	-0.31993205
TXNDC9	-0.70911719
TXNRD1	-0.11551969
VDAC1	-0.42233305

* Average across all 20 knockdown seed gene signatures.

Supplementary Table S10. Enrichr cell pathway analysis (KEGG 2016) of the panel of upregulated genes after iLINCS cluster analysis.

Pathway	p-value	Associated genes
Endocytosis	0.0108	SMAD3; ERBB3; ADRB2; RAB11FIP2; TGFBR2
TGFβ signaling pathway	0.0123	SMAD3; BAMBI; TGFBR2
MAPK signaling pathway	0.0223	DUSP4; PAK1; RASA1; TGFBR2
FoxO signaling pathway	0.0264	SMAD3; FOXO4; TGFBR2
Calcium signaling pathway	0.0541	ERBB3; ADRB2; SLC25A4

Supplementary Table S11. Enrichr cell pathway analysis (KEGG 2016) of the panel of downregulated genes after iLINCS cluster analysis.

Pathway	p-value	Associated genes
Cell cycle	0.0003	CCNB2; PCNA; CDC45; CCNE2; CDK1
p53 signaling pathway	0.0064	CCNB2; CCNE2; CDK1
Pyrimidine metabolism	0.0157	CANT1; TXNRD1; POLR2I

Supplementary Table S12. Enrichr cell pathway analysis (KEGG 2016) of panels of up- and downregulated genes after iLINCS cluster analysis.

Pathway	p-value	Associated genes
Cell cycle	8.33E-05	CCNB2; PCNA; SMAD3; CDC45; CCNE2; CDK1; E2F2
Calcium signaling pathway	0.0265	ERBB3; GNAS; VDAC1; ADRB2; SLC25A4
FoxO signaling pathway	0.0335	CCNB2; SMAD3; FOXO4; TGFBR2
MAPK signaling pathway	0.0375	DUSP4; PAK1; RASA1; STMN1; TGFBR2
Endocytosis	0.0375	SMAD3; ERBB3; ADRB2; RAB11FIP2; TGFBR2

Supplementary Table S13. Top 20 chemical perturbagens anti-correlated with the panel of clustered upregulated genes, ordered by concordance score (drug set 1).

Perturbagen	Mechanism of Action*	Cell Line	Conc.	Time	Concordance	p-value
MAYBRIDGE4_003028	Unknown	A549	10uM	24h	-0.618	< 2.0e-4
Teniposide	Topoisomerase inhibitor	A549	1uM	24h	-0.609	< 2.0e-4
LE-135	Retinoid receptor agonist	THP1	20uM	6h	-0.601	< 2.0e-4
Teniposide	Topoisomerase inhibitor	A549	3uM	24h	-0.599	< 2.0e-4
PD-0325901	MEK inhibitor	HS578T	0.1uM	24h	-0.557	2.0e-4
BAY 59-3074	Unknown	NPC	10uM	24h	-0.549	2.0e-4
CI-1040	MEK inhibitor	HS578T	0.5uM	24h	-0.532	4.0e-4
AZ628	RAF inhibitor	HS578T	10uM	24h	-0.531	4.0e-4
SCHEMBL17857056	FGFR inhibitor	HS578T	0.5uM	24h	-0.524	5.0e-4
BRD-K55681368	Unknown	VCAP	5uM	24h	-0.520	6.0e-4
3-Methyladenine	PI3K inhibitor	RMUGS	10uM	6h	-0.513	7.0e-4
BRD-K72061918	Unknown	PC3	5uM	24h	-0.509	8.0e-4
Aurora A Inhibitor I	Aurora inhibitor	A549	10uM	24h	-0.509	8.0e-4
Trioxsalen	DNA synthesis inhibitor	PC3	10uM	24h	-0.507	8.0e-4
BRD-K11156132	Unknown	VCAP	5uM	6h	-0.502	0.001
PAC-1	Caspase activator	HCC515	10uM	6h	-0.498	0.001
Gefitinib	EGFR inhibitor	MCF10A	0.1uM	6h	-0.497	0.001
BRD-K31542390	Inosine monophosphate dehydrogenase inhibitor	HEPG2	3uM	6h	-0.491	0.001
XMD-16144	Unknown	A549	10uM	6h	-0.485	0.002
10-DEBC	AKT inhibitor	SW620	20uM	6h	-0.484	0.002

* Mechanism of action extracted from L1000FWD (http://amp.pharm.mssm.edu/L1000FWD/)

Supplementary Table S14. Top 20 chemical perturbagens anti-correlated with the panel of clustered downregulated genes, ordered by concordance score (drug set 2).

Perturbagen	Mechanism of Action*	Cell Line	Conc.	Time	Concordance	p-value
CHEMBL3183436	Aurora inhibitor	A549	0.04uM	24h	-0.575	2.0e-4
Enclomiphene	Estrogen receptor antagonist	MCF7	0.37uM	24h	-0.557	3.0e-4
BRD-K33341138	Unknown	VCAP	5uM	24h	-0.555	3.0e-4
BRD-A73558769	Unknown	CD34	0.5uM	6h	-0.532	6.0e-4
BRD-K51556300	Unknown	PC3	3uM	24h	-0.524	7.0e-4
Dexamethasone	Glucocorticoid receptor agonist	A549	10uM	6h	-0.517	9.0e-4
BRD-K02544880	Unknown	VCAP	5uM	24h	-0.506	0.001
BX 912	PDK1 inhibitor	MDAMB231	10uM	6h	-0.502	0.001
Tivozanib	VEGFR inhibitor	RKO	10uM	6h	-0.500	0.001
LRRK2-IN-1	LRRK2 inhibitor	SKBR3	0.5uM	24h	-0.497	0.002
Teniposide	Topoisomerase inhibitor	SW948	1uM	6h	-0.491	0.002
Pramipexole	Dopamine receptor agonist	VCAP	10uM	6h	-0.485	0.002
RG 108	DNA methyltransferase inhibitor	AGS	80uM	6h	-0.484	0.002
BRD-K42614769	Unknown	VCAP	5uM	24h	-0.479	0.002
AM-580	Retinoid receptor agonist	MCF7	10uM	6h	-0.478	0.002
MLS003448149	Unknown	SW620	10uM	6h	-0.478	0.002
AZD-5438	CDK inhibitor	MCF10A	0.1uM	6h	-0.478	0.002
BRD-K05542495	Unknown	HA1E	10uM	6h	-0.475	0.003
CGS 20625	Benzodiazepine receptor agonist	A549	10uM	6h	-0.472	0.003
BRD-K51556300	Unknown	HT29	10uM	6h	-0.470	0.003

* Mechanism of action extracted from L1000FWD (http://amp.pharm.mssm.edu/L1000FWD/)

Supplementary Table S15. Top 20 chemical perturbagens anti-correlated with the panels of clustered up- and downregulated genes, ordered by concordance score (drug set 3).

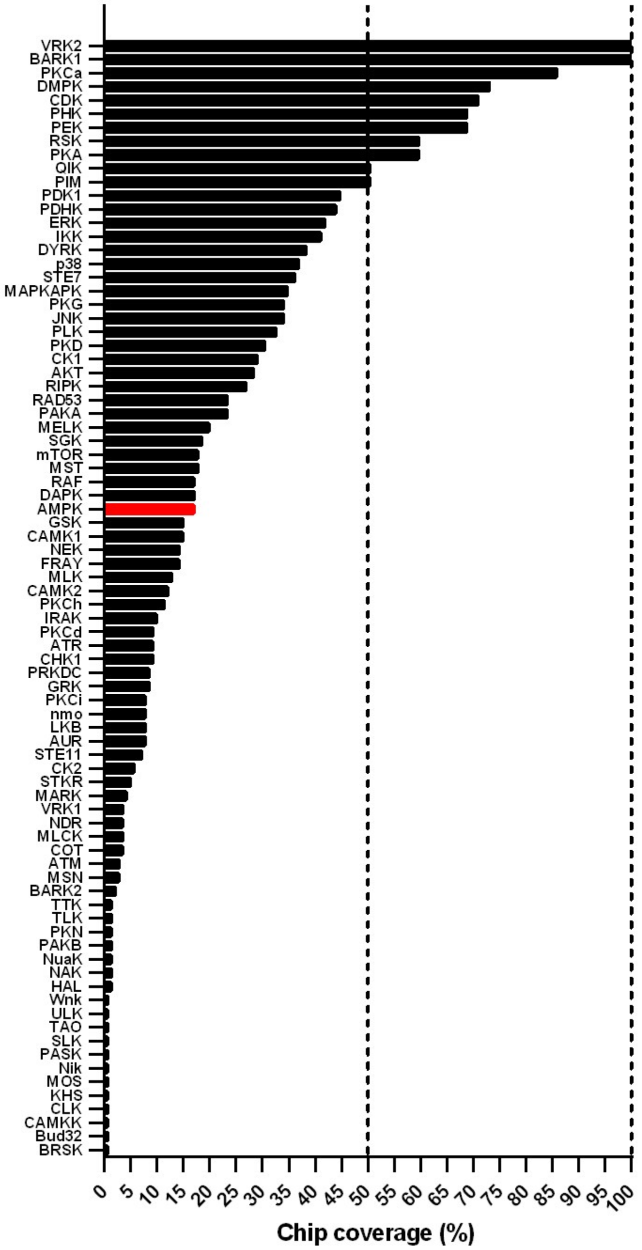
Perturbagen	Mechanism of Action*	Cell Line	Conc.	Time	Concordance	p-value
Fulvestrant	Estrogen receptor antagonist	VCAP	1uM	24h	-0.570	5.0e-8
Erismodegib	Smoothened receptor antagonist	H1299	10uM	6h	-0.496	3.8e-6
Thioridazine	Dopamine receptor antagonist	VCAP	1uM	24h	-0.488	5.7e-6
Promethazine	Histamine receptor antagonist	A549	5uM	24h	-0.480	8.8e-6
BRL54443	Serotonin receptor agonist	HCC515	10uM	6h	-0.468	< 1.0e-4
Trifluoperazine	Dopamine receptor antagonist	VCAP	5uM	24h	-0.465	< 1.0e-4
PD-98059	MEK inhibitor	HT115	10uM	6h	-0.442	1.0e-4
Valproic acid	HDAC inhibitor	VCAP	1uM	6h	-0.437	1.0e-4
Tretinoin	Retinoid receptor agonist	VCAP	1uM	24h	-0.418	1.0e-4
Thioridazine	Dopamine receptor antagonist	VCAP	1uM	6h	-0.406	2.0e-4
Niridazole	Phosphofructokinase inhibitor	MCF7	10uM	24h	-0.398	3.0e-4
Sirolimus	mTOR inhibitor	VCAP	1uM	6h	-0.397	3.0e-4
MLS002725684	Unknown	A549	10uM	24h	-0.392	4.0e-4
Tretinoin	Retinoid receptor agonist	VCAP	1uM	48h	-0.385	5.0e-4
CHEMBL1612418	Unknown	A549	10uM	24h	-0.382	6.0e-4
TSU-68	FGFR inhibitor; PDGFR inhibitor; VEGFR inhibitor	H1299	5uM	6h	-0.377	7.0e-4
FUMONISIN-B1	Unknown	A549	100uM	24h	-0.376	7.0e-4
Genistein	Protein tyrosine kinase inhibitor	VCAP	1uM	24h	-0.375	7.0e-4
ST013886	Unknown	VCAP	1uM	48h	-0.375	7.0e-4
LY-294002	mTOR inhibitor; PI3K inhibitor	VCAP	1uM	48h	-0.365	0.001

* Mechanism of action extracted from L1000FWD (http://amp.pharm.mssm.edu/L1000FWD/)

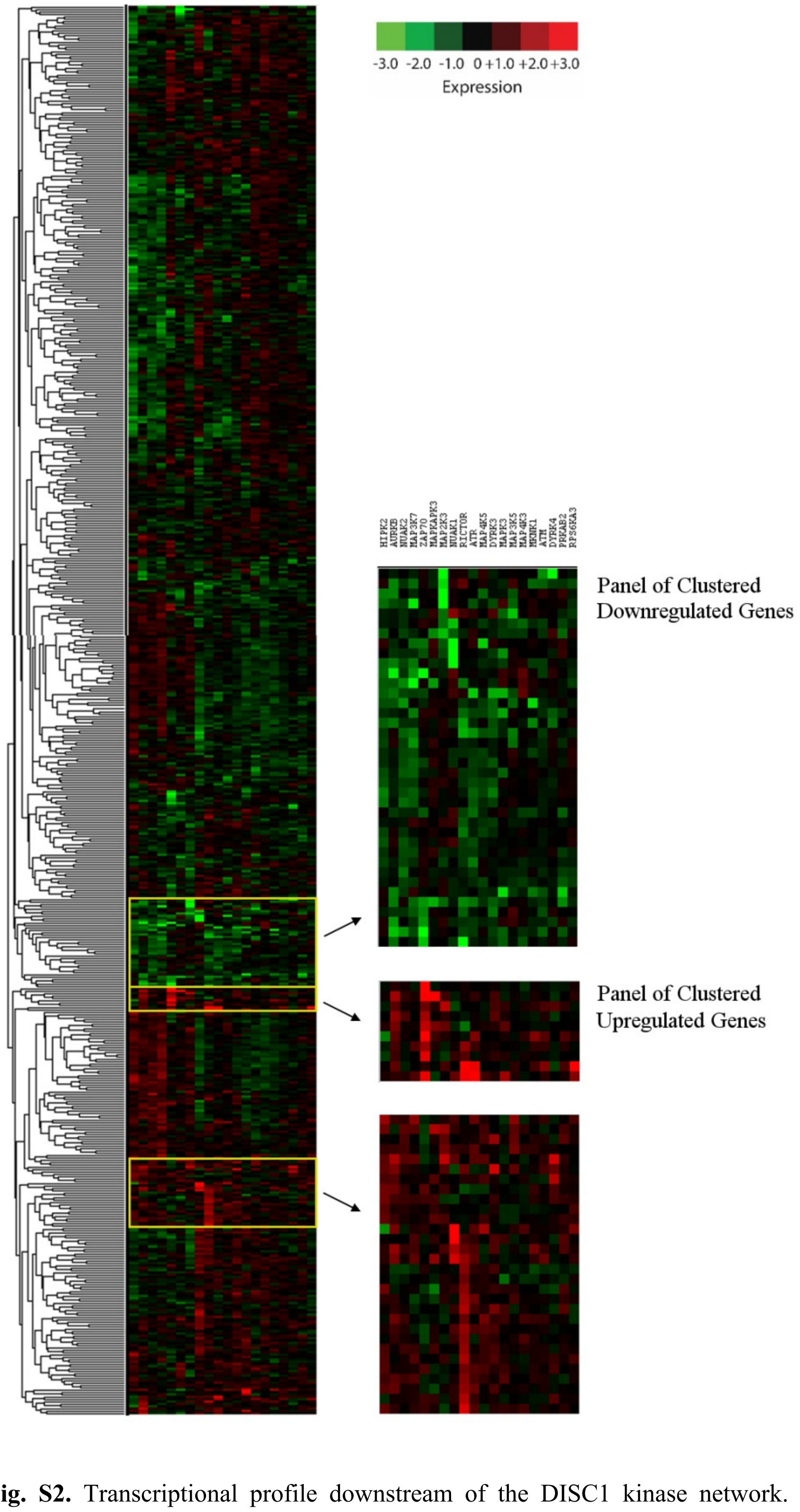
Supplementary Table S16. Top 20 chemical perturbagens anti-correlated with the complete kinase network signature, ordered by concordance score (drug set 4).

Perturbagen	Mechanism of Action*	Cell Line	Conc.	Time	Concordance	p-value
Valproic acid	HDAC inhibitor	VCAP	5uM	48h	-0.243	1.5e-14
Fulvestrant	Estrogen receptor antagonist	VCAP	1uM	24h	-0.214	1.2e-11
Tretinoin	Retinoid receptor agonist	VCAP	1uM	48h	-0.214	1.5e-11
Tretinoin	Retinoid receptor agonist	VCAP	1uM	24h	-0.199	3.7e-10
Valproic acid	HDAC inhibitor	VCAP	1uM	6h	-0.175	3.5e-8
Genistein	Protein tyrosine kinase inhibitor	VCAP	1uM	24h	-0.169	1.1e-7
Troglitazone	PPAR receptor agonist	VCAP	20uM	48h	-0.163	3.1e-7
Genistein	Protein tyrosine kinase inhibitor	VCAP	1uM	6h	-0.161	4.3e-7
Trifluoperazine	Dopamine receptor antagonist	VCAP	1uM	48h	-0.148	3.4e-6
Fluphenazine	Dopamine receptor antagonist	VCAP	1uM	48h	-0.148	3.5e-6
BRD-K38865695	Unknown	VCAP	5uM	6h	-0.140	< 1.0e-4
SA-1456734	Unknown	MCF7	0.5uM	24h	-0.138	< 1.0e-4
AC1O44XP	Unknown	VCAP	1uM	24h	-0.135	< 1.0e-4
Thioridazine	Dopamine receptor antagonist	VCAP	1uM	24h	-0.134	< 1.0e-4
LY-294002	mTOR inhibitor; PI3K inhibitor	VCAP	1uM	48h	-0.134	< 1.0e-4
Tretinoin	Retinoid receptor agonist	VCAP	5uM	6h	-0.133	< 1.0e-4
Fulvestrant	Estrogen receptor antagonist	VCAP	5uM	6h	-0.133	< 1.0e-4
Tretinoin	Retinoid receptor agonist	VCAP	20uM	24h	-0.132	< 1.0e-4
Trifluoperazine	Dopamine receptor antagonist	VCAP	5uM	24h	-0.130	< 1.0e-4
SCHEMBL13991002	Unknown	H1299	40uM	6h	-0.128	1.0e-4

* Mechanism of action extracted from L1000FWD (http://amp.pharm.mssm.edu/L1000FWD/)



Supplementary Fig. S1. Kinase mapping distribution for the reporter peptides of the PamGene kinome array. For each reporter peptide, a list of kinases was generated that are most likely to phosphorylate the specific phosphosites using prediction algorithms (GPS 3.0 and Kinexus Phosphonet) and data extracted from literature (using public databases, PhosphoELM and PhosphoSite Plus). The graph shows the frequency distribution of kinases predicted to act across the different peptide substrates of the chip. AMPK is highlight as an example, being mapped on 17.02% of peptide substrates of the kinome array.



Supplementary Fig. S2. Transcriptional profile downstream of the DISC1 kinase network. iLINCS clustering analysis identified a panel of upregulated and downregulated genes across all knockdown signatures of the DISC1 kinase network seed genes (boxed on heatmap).

SUPPLEMENTARY METHODS

Quantitative analysis of proteome by multiplexed TMT-LC/LC-MS/MS

Quantitative proteomics analysis was performed by the tandem mass tagging (TMT) strategy. In brief, 4-week-old hiPSC-derived cortical neurons were collected and homogenized in buffer (8 M urea, 50 mM HEPES, pH 8.5) on ice. After quantification by BCA assay (Thermo Fisher Scientific) and protein integrity evaluation by SDS-PAGE, 200 µg protein aliquots from each sample were adjusted to 4 µg/µL by digestion buffer supplemented with 10% acetonitrile and 4 mM dithiothreitol. Digestion was performed in the presence of 2 µg Lys-C (Wako, 1:100 w/w) at room temperature for 2 h, and then in diluted 2 M urea digestion buffer supplemented with 4 µg trypsin (Promega, 1:50 w/w) for an additional 4 h at room temperature, before quenching with 1% trifluoroacetic acid. The peptides were then desalted and labeled by TMT reagents (TMT10plex™ Isobaric Label Reagent Set, cat#90110, Thermo Fisher Scientific). Equally mixed TMT-labeled peptides from all samples were desalted and then fractionated by basic pH HPLC on a C18 column (XBridge, 3.5 µm particle size, 4.6 mm × 25 cm, Waters) at a flow rate of 0.4 mL/min. Each fractionated peptide sample was then run by a long gradient (15% to 55%) acidic pH HPLC followed by tandem MS analysis with a Q Exactive hybrid Quadrupole-Orbitrap (Thermo Fisher Scientific), operated in data-dependent mode with a survey MS scan (60,000 resolution, 2 × 105 AGC target and 50 ms maximal ion time) followed by MS/MS scans (60,000 resolution, 1 × 105 AGC target, 150 ms maximal ion time, HCD, 38% collision energy (stepped: 5%), 1.2 m/z isolation window and 0.25 m/z offset, and 45 s dynamic exclusion). The acquired MS/MS raw files were first converted into the mzXML format and then searched by JUMP software (version 1.12.1) against the integrated target database from UniProt with a decoy database (reversed sequences of all proteins in the target database). As a result, ~9000 unique proteins were identified at 1% FDR (0.1% unique peptide FDR and 0.05% PSM FDR). The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE (Perez-Riverol Y, et al. 2019) partner repository with the dataset identifier PXD013391.