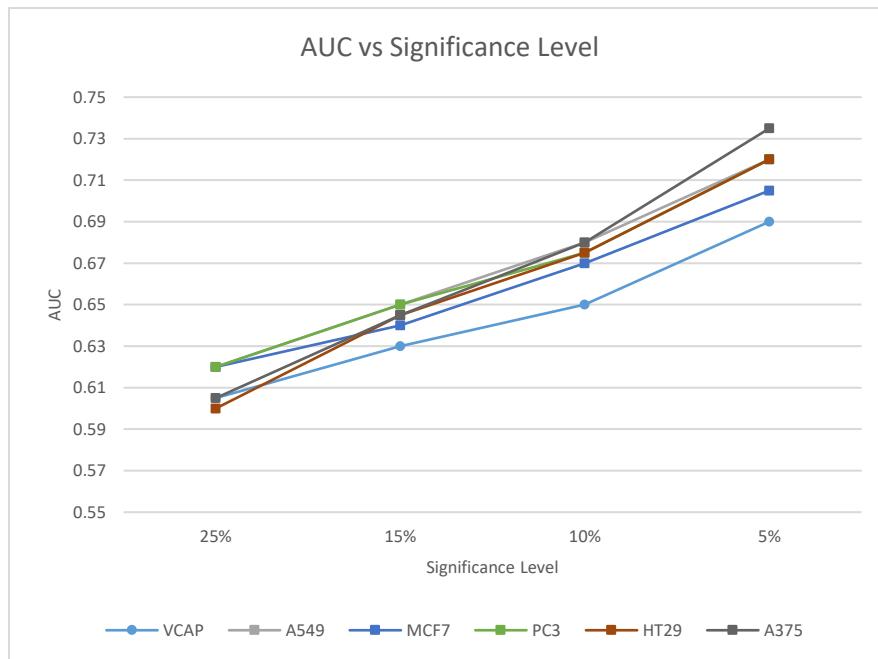


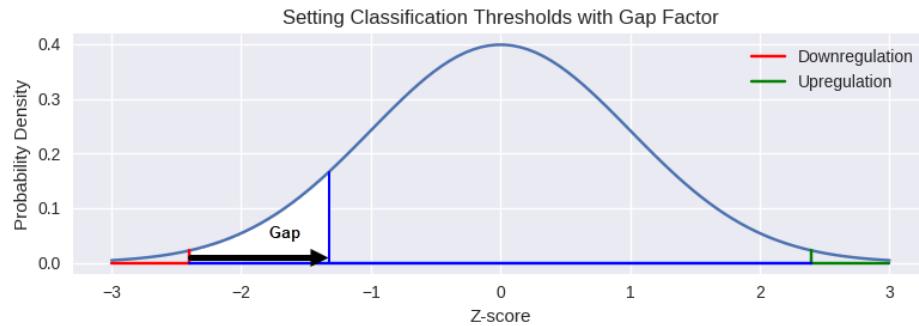
Supplementary Table 1. Comparing Significance Level Thresholds. Early in the study we compared the effect of changing the significance levels on prediction scores. We compiled the prediction scores of the cell lines available in Phase 1 of LINCS dataset for 5%, 10%, 15%, and 25% significance levels. Note that some hyper-parameters may have changed.

Cell Line	Significance Level AUC			
	25%	15%	10%	5%
VCAP	0.605	0.63	0.65	0.69
HCC515	0.675	0.69	0.71	0.745
A549	0.62	0.65	0.68	0.72
HEPG2	0.72	0.74	0.765	0.81
MCF7	0.62	0.64	0.67	0.705
PC3	0.62	0.65	0.675	0.72
HEK293T	0.685	0.735	0.72	0.78
HT29	0.6	0.645	0.675	0.72
A375	0.605	0.645	0.68	0.735
HA1E	0.63	0.65	0.685	0.72
THP1	0.655	0.68	0.705	0.73
BT20	0.61	0.65	0.665	0.705
U937	0.595	0.635	0.69	0.71
MCF10A	0.68	0.665	0.705	0.73
HUH7	0.71	0.77	0.775	0.81
NKDBA	0.645	0.685	0.71	0.74
NOMO1	0.685	0.74	0.74	0.79
JURKAT	0.66	0.76	0.735	0.855
SKBR3	0.61	0.65	0.68	0.715
HS578T	0.62	0.64	0.685	0.75
MDAMB231	0.655	0.68	0.72	0.755
HL60	0.77	0.8	0.86	0.915
U266	0.725	0.845	0.805	0.935

Supplementary Figure 1. AUC vs Significance Level. This graph shows the plot of the AUC scores of the 6 cell lines used in the paper with data from Supplementary Table 1. As the significance level decreases, higher AUC scores are achieved.



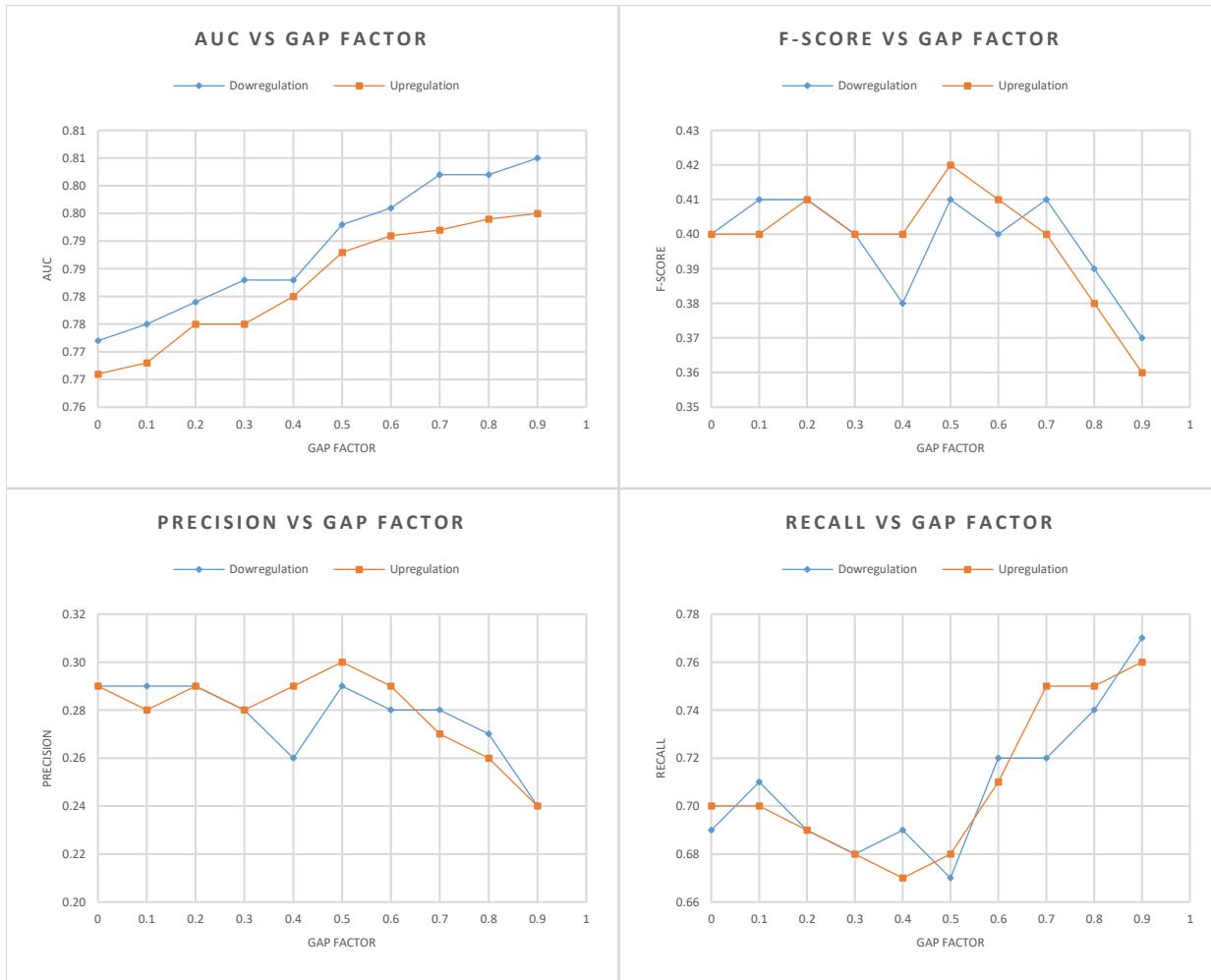
Supplementary Figure 2. Gap Factor Analysis. Illustration of how we exclude samples with *z-scores* that fell within the range of the gap between the threshold and a percentage of the distance between the threshold and the mean with the goal of removing ambiguity between classes.



Supplementary Table 2. Gap Analysis. This table shows results of early work on the effects of gap factor on AUC along with other prediction measures: precision, recall and F-score for an example cell line MCF7. Note that some hyper-parameters may have changed.

Gap Factor	Down Regulation				Up Regulation			
	AUC	Precision	Recall	F-score	AUC	Precision	Recall	F-score
0	0.772	0.29	0.69	0.4	0.766	0.29	0.7	0.4
0.1	0.775	0.29	0.71	0.41	0.768	0.28	0.7	0.4
0.2	0.779	0.29	0.69	0.41	0.775	0.29	0.69	0.41
0.3	0.783	0.28	0.68	0.4	0.775	0.28	0.68	0.4
0.4	0.783	0.26	0.69	0.38	0.78	0.29	0.67	0.4
0.5	0.793	0.29	0.67	0.41	0.788	0.3	0.68	0.42
0.6	0.796	0.28	0.72	0.4	0.791	0.29	0.71	0.41
0.7	0.802	0.28	0.72	0.41	0.792	0.27	0.75	0.4
0.8	0.802	0.27	0.74	0.39	0.794	0.26	0.75	0.38
0.9	0.805	0.24	0.77	0.37	0.795	0.24	0.76	0.36

Supplementary Figure 3. AUC vs Significance Level. We plotted the data from Supplementary Table 2. As gap factor increases AUC increases at that cost of decreased chemical diversity. Precision, recall and F-score stay relatively the same at lower gap factors.



Supplementary Table 3. LNCaP RNA-Seq Prediction F-score Comparison. Below are the F-score values calculated from LINCS LNCaP 10-fold cross validation training results. We compared the RNA-Seq prediction F-score values to the values obtained from the LINCS training set. RNA-Seq prediction F-score was found to be significantly lower (p-values < 0.02) than the F-score obtained from training the model on the LINCS training set.

LNCaP F-score		X10 3H		X10 24H	
Fold		Down	Up	Down	Up
1		0.351	0.366	0.438	0.504
2		0.354	0.358	0.498	0.519
3		0.335	0.218	0.508	0.536
4		0.297	0.391	0.426	0.458
5		0.367	0.430	0.540	0.473
6		0.323	0.413	0.480	0.413
7		0.372	0.365	0.492	0.531
8		0.326	0.317	0.512	0.446
9		0.386	0.302	0.530	0.458
10		0.326	0.294	0.519	0.503
Mean		0.344	0.345	0.494	0.484
Stdev		0.026	0.060	0.035	0.039
RNA-Seq Pred Fscore		0.084	0.145	0.053	0.025
Zscore		-10.123	-3.330	-12.477	-11.898
P-value		2.2E-23	1.6E-03	6.3E-35	7.2E-32

Supplementary Table 4 and 5. Confusion Matrices calculated from predicting RNA-Seq data using the 10 cross validation upregulation and downregulation models trained on 10µM 3H LNCaP perturbation data from LINCS.

10µM 3H Upregulation			Confusion Matrix			10µM 3H Downregulation			Confusion Matrix		
Fold	AUC	F-score	Predicted Class	Actual 1	Actual 0	Fold	AUC	F-score	Predicted Class	Actual 1	Actual 0
1	0.937	0.125	1	3	200	1	0.671	0.056	1	5	224
			0	2	2690				0	13	2653
2	0.924	0.200	1	3	250	2	0.676	0.128	1	6	271
			0	2	2640				0	12	2606
3	0.783	0.077	1	1	186	3	0.733	0.100	1	7	200
			0	4	2704				0	11	2677
4	0.684	0.118	1	1	126	4	0.662	0.128	1	6	226
			0	4	2764				0	12	2651
5	0.940	0.083	1	3	200	5	0.748	0.062	1	10	379
			0	2	2690				0	8	2498
6	0.948	0.286	1	4	247	6	0.616	0.091	1	5	236
			0	1	2643				0	13	2641
7	0.816	0.111	1	3	342	7	0.711	0.087	1	3	129
			0	2	2548				0	15	2748
8	0.857	0.182	1	2	207	8	0.591	0.058	1	6	258
			0	3	2683				0	12	2619
9	0.752	0.182	1	3	202	9	0.737	0.077	1	4	158
			0	2	2688				0	14	2719
10	0.865	0.083	1	3	380	10	0.694	0.049	1	4	286
			0	2	2510				0	14	2591
Avg	0.851	0.145				Avg	0.684	0.084			

Supplementary Table 6 and 7. Confusion Matrices calculated from predicting RNA-Seq data using the 10 cross validation upregulation and downregulation models trained on 10 μ M 24H LNCaP perturbation data from LINCS.

10 μ M 24H Upregulation			Confusion Matrix			10 μ M 24H Downregulation			Confusion Matrix		
Fold	AUC	F-score	Predicted Class	Actual 1	Actual 0	Fold	AUC	F-score	Predicted Class	Actual 1	Actual 0
1	0.850	0.046	1	2	523	1	0.742	0.081	1	9	634
			0	3	2367				0	9	2243
2	0.644	0.042	1	2	751	2	0.757	0.059	1	8	665
			0	3	2139				0	10	2212
3	0.563	0.012	1	2	718	3	0.724	0.059	1	10	682
			0	3	2175				0	8	2195
4	0.604	0.011	1	2	639	4	0.680	0.050	1	12	1456
			0	3	2251				0	6	1421
5	0.589	0.007	1	1	615	5	0.758	0.043	1	10	621
			0	4	2275				0	8	2256
6	0.629	0.020	1	2	1239	6	0.753	0.050	1	10	551
			0	3	1651				0	8	2326
7	0.678	0.026	1	2	775	7	0.734	0.044	1	7	566
			0	3	2115				0	11	2311
8	0.564	0.017	1	2	788	8	0.721	0.039	1	7	565
			0	3	2102				0	11	2312
9	0.779	0.029	1	2	605	9	0.744	0.049	1	9	435
			0	3	2285				0	9	2442
10	0.760	0.044	1	2	668	10	0.707	0.052	1	9	652
			0	3	2222				0	9	2225
Avg	0.666	0.025				Avg	0.732	0.053			

Supplementary Table 8. Comparison of performance measures between DeepCOP and Random Forest.

Cell Line	DeepCOP						Random Forest					
	Down Regulation			Up Regulation			Down Regulation			Up Regulation		
	AUC	Fscore	E _f	AUC	Fscore	E _f	AUC	Fscore	E _f	AUC	Fscore	E _f
PC3	0.84	0.36	8.44	0.84	0.36	8.56	0.71	0.21	3.50	0.71	0.21	3.48
MCF7	0.84	0.38	8.82	0.84	0.39	8.86	0.72	0.21	3.51	0.72	0.21	3.54
VCAP	0.84	0.36	8.28	0.84	0.36	8.27	0.70	0.18	2.93	0.70	0.18	2.92
A549	0.81	0.34	6.14	0.81	0.34	6.03	0.68	0.20	2.64	0.68	0.20	2.62
A375	0.82	0.40	6.23	0.83	0.40	6.28	0.71	0.25	3.08	0.71	0.25	3.12
HT29	0.81	0.36	6.15	0.81	0.36	6.48	0.70	0.23	3.02	0.70	0.23	2.99