

Table S1 Related to Figure 4: Datasets used in this study

	Number of genes (<i>g</i>)	Number of samples / cells	Title
Grun 2015	23,630	192	Single-Cell mRNA Sequencing Reveals Rare Intestinal Cell Types
GTEx	14,202*	8,555	The Genotype-Tissue Expression (GTEx) pilot analysis: multi-tissue gene regulation in humans
ImmGen	24,922	214	Conservation and divergence in the transcriptional programs of the human and mouse immune systems
Tasic 2016	24,057	1,809	Adult mouse cortical cell taxonomy by single cell transcriptomics
Thomsen 2016	23,045	45	Fixed single-cell transcriptomic characterization of human radial glial diversity
Zeisel 2015	19,972	3,005	Single-cell RNA-seq of mouse cerebral cortex
PerturbSeq	11,738	49,234	Perturb-Seq: Dissecting Molecular Circuits with Scalable Single-cell RNA Profiling of Pooled Genetic Screens
TCGA	20,531	10,554	The Cancer Genome Atlas
TCGA_GBMLGG	20,531	696	The Cancer Genome Atlas - Glioblastoma and low grade glioma
TCGA_KICH	20,531	66	The Cancer Genome Atlas - Kidney Chromophobe
TCGA_READ	20,531	95	The Cancer Genome Atlas - Rectum adenocarcinoma
TCGA_CESC	20,531	306	The Cancer Genome Atlas - Cervical squamous cell carcinoma and endocervical adenocarcinoma
TCGA_PAAD	20,531	179	The Cancer Genome Atlas - Pancreatic adenocarcinoma
TCGA_THYM	20,531	120	The Cancer Genome Atlas - Thymoma
TCGA_PCPG	20,531	184	The Cancer Genome Atlas - Pheochromocytoma and Paraganglioma
TCGA_BRCA	20,531	1,100	The Cancer Genome Atlas - Breast invasive carcinoma
TCGA_UCS	20,531	57	The Cancer Genome Atlas - Uterine Carcinosarcoma
TCGA_KIPAN	20,531	891	The Cancer Genome Atlas - Pan kidney
TCGA_THCA	20,531	509	The Cancer Genome Atlas - Thyroid carcinoma
TCGA_HNSC	20,531	522	The Cancer Genome Atlas - Head and Neck squamous cell carcinoma
TCGA_ACC	20,531	79	The Cancer Genome Atlas - Adrenocortical carcinoma
TCGA_TGCT	20,531	156	The Cancer Genome Atlas - Testicular Germ Cell Tumors
TCGA_LUSC	20,531	501	The Cancer Genome Atlas - Lung squamous cell carcinoma
TCGA_KIRC	20,531	534	The Cancer Genome Atlas - Kidney renal clear cell carcinoma
TCGA_BLCA	20,531	408	The Cancer Genome Atlas - Bladder Urothelial Carcinoma
TCGA_SARC	20,531	262	The Cancer Genome Atlas - Sarcoma
TCGA_UVM	20,531	80	The Cancer Genome Atlas - Uveal Melanoma
TCGA_CHOL	20,531	36	The Cancer Genome Atlas - Cholangiocarcinoma
TCGA_LUAD	20,531	517	The Cancer Genome Atlas - Lung adenocarcinoma
TCGA_DLBC	20,531	28	The Cancer Genome Atlas - Lymphoid Neoplasm Diffuse Large B-cell Lymphoma
TCGA_UCEC	20,531	177	The Cancer Genome Atlas - Uterine Corpus Endometrial Carcinoma
TCGA_MESO	20,531	86	The Cancer Genome Atlas - Mesothelioma
TCGA_COADRE/	20,531	382	The Cancer Genome Atlas - Colorectal adenocarcinoma
TCGA_OV	20,531	265	The Cancer Genome Atlas - Ovarian serous cystadenocarcinoma

TCGA_GBM	20,531	166	The Cancer Genome Atlas - Glioblastoma multiforme
TCGA_PRAD	20,531	498	The Cancer Genome Atlas - Prostate adenocarcinoma
TCGA_KIRP	20,531	291	The Cancer Genome Atlas - Kidney renal papillary cell carcinoma
TCGA_LIHC	20,531	373	The Cancer Genome Atlas - Liver hepatocellular carcinoma
TCGA_LAML	20,531	173	The Cancer Genome Atlas - Acute Myeloid Leukemia
TCGA_LGG	20,531	530	The Cancer Genome Atlas - Brain Lower Grade Glioma
TCGA_COAD	20,531	287	The Cancer Genome Atlas - Colon adenocarcinoma

Table S2 Related to Figure 4: Matrix factorization statistics

Dataset	SVD fit	SVD modules	avg SVD module size	avg active SVD modules
ImmGen	99.5%	65	8,051.0	18.1
Thomsen_2016	99.5%	37	5,498.9	10.9
GTEX	99.5%	740	5,335.9	202.3
TCGA_GBMLGG	99.5%	502	7,313.8	193.2
TCGA_LUAD	99.5%	438	7,418.6	201.9
TCGA_READ	99.5%	86	7,449.5	42.4
TCGA_MESO	99.5%	78	7,447.4	38.7
TCGA_BLCA	99.5%	355	7,418.7	168.9
TCGA_KIPAN	99.5%	607	7,309.7	227.5
TCGA_PCPG	99.5%	158	7,404.0	70.8
TCGA_PAAD	99.5%	148	7,329.7	63.7
TCGA_CHOL	99.3%	33	7,487.5	17.0
TCGA_UCEC	99.5%	156	7,401.0	73.4
TCGA_COADREAD	99.5%	325	7,427.7	145.8
TCGA_LIHC	99.5%	317	7,393.9	144.6
TCGA_ACC	99.5%	72	7,471.1	35.7
TCGA_UVM	99.5%	68	7,340.0	29.5
TCGA_LAML	99.5%	145	7,382.7	61.2
TCGA_GBM	99.5%	143	7,373.8	64.2
TCGA_BRCA	99.5%	861	7,384.0	387.9
TCGA_TGCT	99.5%	131	7,350.9	55.6
TCGA_CESC	99.5%	267	7,426.5	126.8
TCGA_KICH	99.4%	57	7,373.2	25.7
Grun_2015	99.5%	145	7,539.7	58.9
TCGA_DLBC	99.4%	26	7,478.1	13.5
TCGA_COAD	99.5%	248	7,431.4	112.9
TCGA_KIRP	99.5%	225	7,379.3	91.9
TCGA_OV	99.5%	241	7,468.8	122.8
TCGA_THYM	99.5%	89	7,162.1	32.1
TCGA_UCS	99.5%	54	7,490.8	28.6
Tasic_2016	98.4%	1,000	7,621.5	489.8
TCGA_SARC	99.5%	231	7,415.2	110.5
TCGA_KIRC	99.5%	397	7,320.3	157.3
TCGA_LGG	99.5%	394	7,320.2	153.7
TCGA_HNSC	99.5%	434	7,393.1	196.2
TCGA_THCA	99.5%	378	7,285.8	143.0
TCGA_LUSC	99.5%	431	7,434.9	205.5
TCGA_PRAD	99.5%	391	7,314.9	159.7
TCGA	94.4%	1,000	10,057.0	447.7
Zeisel_2015	93.8%	1,000	8,781.5	539.5

Dataset	sprse NMF fit	sNMF modules	avg sNMF module size	avg active sNMF modules
ImmGen	99.0%	93	7,714.5	3.8
Thomsen_2016	99.1%	37	2,348.8	3.8
GTEX	81.5%	1,082	3,933.7	5.8
TCGA_GBMLGG	93.0%	502	7,040.7	6.8
TCGA_LUAD	90.2%	438	6,746.5	6.1
TCGA_READ	97.6%	86	7,061.2	3.4
TCGA_MESO	98.2%	78	6,921.9	3.8
TCGA_BLCA	91.7%	355	6,769.2	5.7
TCGA_KIPAN	50.2%	607	8,225.7	2.2
TCGA_PCPG	92.7%	158	7,293.7	3.6
TCGA_PAAD	88.0%	148	7,477.9	3.3
TCGA_CHOL	97.9%	33	6,672.4	3.5
TCGA_UCEC	96.8%	156	7,000.8	4.4
TCGA_COADREAD	91.6%	325	6,946.0	5.6
TCGA_LIHC	95.0%	317	6,669.8	6.4
TCGA_ACC	96.8%	72	6,731.9	3.6
TCGA_UVM	98.4%	68	7,224.0	3.4
TCGA_LAML	90.9%	145	7,126.3	3.5
TCGA_GBM	94.2%	143	6,954.0	4.3
TCGA_BRCA	91.7%	861	6,948.0	8.0
TCGA_TGCT	97.6%	131	7,028.3	4.1
TCGA_CESC	89.9%	267	7,048.5	5.0
TCGA_KICH	98.9%	57	7,286.8	3.4
Grun_2015	94.6%	145	2,986.2	8.4
TCGA_DLBC	99.1%	26	7,064.9	2.9
TCGA_COAD	90.9%	248	6,922.3	4.7
TCGA_KIRP	95.1%	225	7,020.7	5.9
TCGA_OV	80.6%	241	7,207.3	3.0
TCGA_THYM	98.0%	89	7,216.0	4.5
TCGA_UCS	98.3%	54	6,969.3	3.0
Tasic_2016	50.4%	1,000	2,265.8	5.7
TCGA_SARC	85.4%	231	7,020.0	3.8
TCGA_KIRC	93.1%	397	7,117.3	6.7
TCGA_LGG	94.0%	394	7,013.5	6.6
TCGA_HNSC	45.6%	434	8,154.7	1.6
TCGA_THCA	93.9%	378	7,007.5	6.5
TCGA_LUSC	90.5%	431	6,888.8	5.7
TCGA_PRAD	94.0%	391	6,981.7	6.5
TCGA	85.8%	1,100	7,021.9	14.8
Zeisel_2015	33.5%	1,100	2,564.4	9.9

Dataset	SMAF fit	SMAF modules	avg SMAF module size	avg active SMAF modules
ImmGen	98.4%	152	654.6	6.6
Thomsen_2016	98.3%	48	605.4	6.3
GTEX	97.9%	863	1,321.8	8.1
TCGA_GBMLGG	95.3%	280	5,162.4	8.2
TCGA_LUAD	95.1%	349	4,274.5	7.9
TCGA_READ	94.7%	106	2,092.1	7.5
TCGA_MESO	94.3%	99	1,697.5	6.8
TCGA_BLCA	94.2%	286	3,394.2	7.8
TCGA_KIPAN	94.2%	314	3,399.2	8.2
TCGA_PCPG	94.1%	167	1,717.6	7.3
TCGA_PAAD	94.0%	152	1,430.8	7.1
TCGA_CHOL	94.0%	43	1,910.5	6.1
TCGA_UCEC	93.9%	158	1,997.8	7.2
TCGA_COADREAD	93.9%	269	2,882.7	8.2
TCGA_LIHC	93.8%	265	2,541.5	7.8
TCGA_ACC	93.8%	91	1,797.9	7.2
TCGA_UVM	93.6%	78	1,320.6	6.7
TCGA_LAML	93.5%	134	1,694.9	7.8
TCGA_GBM	93.5%	159	1,354.0	7.5
TCGA_BRCA	93.4%	485	5,910.7	8.2
TCGA_TGCT	93.0%	129	1,241.9	6.8
TCGA_CESC	92.8%	255	1,741.9	7.6
TCGA_KICH	92.4%	69	1,267.5	6.4
Grun_2015	92.4%	116	2,446.9	7.6
TCGA_DLBC	92.3%	31	1,840.1	6.5
TCGA_COAD	92.2%	231	1,683.5	7.9
TCGA_KIRP	92.2%	204	1,308.3	7.8
TCGA_OV	92.1%	253	1,634.4	7.4
TCGA_THYM	91.8%	93	726.2	6.1
TCGA_UCS	91.8%	64	1,615.9	6.4
Tasic_2016	91.7%	560	2,394.9	7.7
TCGA_SARC	91.7%	214	1,324.9	7.1
TCGA_KIRC	91.3%	288	1,139.8	7.8
TCGA_LGG	91.2%	254	1,160.1	7.6
TCGA_HNSC	91.1%	342	1,558.4	7.9
TCGA_THCA	90.9%	271	889.5	8.0
TCGA_LUSC	90.9%	339	1,758.5	7.9
TCGA_PRAD	90.7%	256	1,275.3	7.6
TCGA	87.7%	883	6,922.5	8.5
Zeisel_2015	84.2%	574	4,355.5	8.1

Table S3 Related to Figure 1: Correlation of RNA-Seq and composite qPCR

Parameter	Individual Probe Test (Concentration = 25nM)	Individual Probe Test (Concentration = 2.5nM)	Individual Probe Test (Concentration = 250pM)	Individual Probe Test (Concentration = 25pM)
Pearson r	0.1485	0.1874	0.4963	0.623
95% confidence interval	-0.2306 to 0.4885	-0.1924 to 0.5184	0.1586 to 0.7301	0.3324 to 0.8056
P value (two-tailed)	0.4419	0.3303	0.0062	0.0003
P value summary	ns	ns	**	***
Is the correlation significant? (alpha=0.05)	No	No	Yes	Yes
R square	0.02206	0.03512	0.2463	0.3882
Spearman r	0.1338	0.3101	0.5286	0.6433
95% confidence interval	-0.2554 to 0.4858	-0.07501 to 0.6148	0.1901 to 0.7548	0.3523 to 0.8209
P value (two-tailed)	0.4888	0.1016	0.0032	0.0002
P value summary	ns	ns	**	***
Exact or approximate P value?	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation	Gaussian Approximation
Is the correlation significant? (alpha=0.05)	No	No	Yes	Yes

Parameter	Individual Gene Test, Four Probes Per Gene (Concentration = 25nM)	Individual Gene Test, Four Probes Per Gene (Concentration = 2.5nM)	Individual Gene Test, Four Probes Per Gene (Concentration = 250pM)	Individual Gene Test, Four Probes Per Gene (Concentration = 25pM)
Pearson r	0.6013	0.3955	0.8834	0.8646
95% confidence interval	-0.1796 to 0.9173	-0.4288 to 0.8604	0.4732 to 0.9788	0.4091 to 0.9752
P value (two-tailed)	0.1149	0.3321	0.0036	0.0056
P value summary	ns	ns	**	**
Is the correlation significant? (alpha=0.05)	No	No	Yes	Yes
R square	0.3616	0.1564	0.7804	0.7475
Spearman r	0.5714	0.4286	0.6429	0.7619
P value (two-tailed)	0.1511	0.2992	0.0962	0.0368
P value summary	ns	ns	ns	*
Exact or approximate P value?	Exact	Exact	Exact	Exact
Is the correlation significant? (alpha=0.05)	No	No	No	Yes

Parameter	Expected vs. Experimental(Rep1)	Expected vs. Experimental(Rep2)

Pearson r	0.8518	0.9014
95% confidence interval	0.6483 to 0.9417	0.7571 to 0.9618
P value (two-tailed)	< 0.0001	< 0.0001
P value summary	***	***
Is the correlation significant? (alpha=0.05)	Yes	Yes
R square	0.7255	0.8124
Spearman r	0.6596	0.6789
95% confidence interval	0.2799 to 0.8609	0.3118 to 0.8697
P value (two-tailed)	0.0021	0.0014
P value summary	**	**
Exact or approximate P value?	Gaussian Approximation	Gaussian Approximation
Is the correlation significant? (alpha=0.05)	Yes	Yes

Table S4 Related to Figure 1: Weights in random composite measurements

Gene ID	Gene Symbol	Measurement 1	Measurement 2	Measurement 3	Measurement 4	Measurement 5	Measurement 6
1	ACTB	1	0.01	0.01	0.01	0.001	0.001
2	EMR1	1	0.001	0.1	0.1	1	0.01
3	GCLC	0.1	0.1	0.001	0.001	0.1	0.01
4	LARS	0.1	0.001	0.1	0.001	0.1	0.1
5	MYB	0.01	0.001	0.001	0.01	0.001	1
6	PDLIM5	0.01	1	1	0.1	0.001	0.1
7	SNAP23	0.1	0.1	0.1	1	0.01	0.01
8	TFRC	0.01	0.1	0.1	0.01	1	0.001
9	ALOX5	0.001	0.001	0.01	0.001	0.01	1
10	FOXK2	0.001	0.001	1	0.01	0.01	0.1
11	HSPA13	1	0.01	1	1	1	0.1
12	MCM4	0.001	0.1	0.001	0.1	0.01	0.01
13	MYC	0.001	0.01	0.01	0.1	0.1	1
14	PFDN5	0.01	1	0.01	0.1	0.001	0.1
15	SRM	0.01	0.01	1	0.01	1	0.1
16	XRCC6	1	1	0.01	1	1	0.01
17	CTSS	0.001	0.001	0.1	1	0.001	0.001
18	GAS7	1	0.01	0.001	1	0.1	0.01
19	HSPA9	0.1	1	1	0.001	0.01	1
20	MDM1	0.1	0.1	0.01	0.001	0.001	0.001
21	OAZ1	0.01	0.01	0.1	0.001	0.1	0.001
22	PLEK	0.1	0.1	0.001	0.01	0.1	0.001
23	STAU1	0.001	1	0.001	0.1	0.01	1

*Values represent the relative abundance of probes for each gene within a measurement

Measurement 7	Measurement 8	Measurement 9	Measurement 10	Measurement 11	Measurement 12	Measurement 13
0.01	1	0.1	1	1	0.01	0.1
0.001	0.01	1	0.01	0.01	0.001	0.001
1	0.1	0.01	0.1	0.001	0.1	0.01
0.01	0.001	0.01	0.01	1	0.001	1
1	0.1	0.001	0.1	0.001	0.01	0.1
0.001	0.1	0.1	0.001	1	1	0.001
0.1	0.1	0.001	0.01	0.001	1	0.001
0.001	1	0.001	0.1	0.001	0.1	0.01
0.01	0.01	0.1	0.01	0.01	0.001	0.01
1	0.01	1	0.1	0.01	0.01	0.1
0.001	0.1	1	0.1	1	0.01	0.01
0.1	0.01	0.001	0.001	0.1	0.1	0.1
0.1	1	0.01	1	0.1	0.001	1
0.1	0.001	1	1	0.01	1	0.01
0.01	0.01	0.001	0.001	0.1	1	0.001
0.001	0.001	0.1	0.001	0.001	0.01	0.1
0.1	0.001	0.001	0.1	0.01	0.1	0.1
0.01	1	0.01	0.001	1	0.01	0.001
1	0.01	0.1	0.01	0.1	0.1	1
0.01	0.001	0.01	0.001	0.1	0.1	1
1	0.1	1	1	0.01	1	1
0.1	0.001	0.01	1	0.001	0.001	0.01
0.001	1	0.1	0.01	0.1	0.001	0.001

Measurement 14	Measurement 15	Measurement 16	Measurement 17	Measurement 18	Measurement 19	Measurement 20
0.001	1	0.001	0.001	1	1	0.1
1	0.001	0.1	0.01	0.001	0.1	1
1	0.01	0.001	0.1	0.001	0.1	1
0.001	0.01	0.1	1	1	1	1
0.1	0.01	0.01	0.001	0.01	0.001	0.01
0.001	0.001	0.1	0.001	0.01	0.001	0.01
0.01	0.001	0.001	0.01	0.01	0.1	1
0.001	1	0.01	0.1	0.01	0.01	0.01
0.001	0.01	0.001	0.1	0.1	0.001	0.001
1	0.001	0.01	0.01	0.01	0.001	0.01
0.1	0.1	0.1	0.01	1	1	0.001
0.01	1	0.1	0.1	1	0.001	0.01
0.01	0.001	1	1	0.001	0.01	0.1
0.01	0.01	0.001	1	0.001	0.01	0.1
0.1	1	0.01	0.01	0.1	0.1	0.001
0.1	1	0.1	0.001	0.001	0.1	0.001
0.01	0.001	0.01	1	0.01	0.1	0.1
0.001	0.01	0.001	0.1	1	1	0.001
1	0.1	1	0.1	0.1	0.001	0.1
1	0.1	1	1	0.001	0.01	0.01
0.01	0.1	0.01	0.001	0.1	1	0.001
0.1	0.1	1	0.01	0.1	0.01	1
0.1	0.1	1	0.001	0.1	0.01	0.1