SUPPORTING ONLINE MATERIALS FOR:

SigCom LINCS: Data and Metadata Search Engine for a Million Gene Expression Signatures

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SUPPORTING FIGURES

Fig. S1

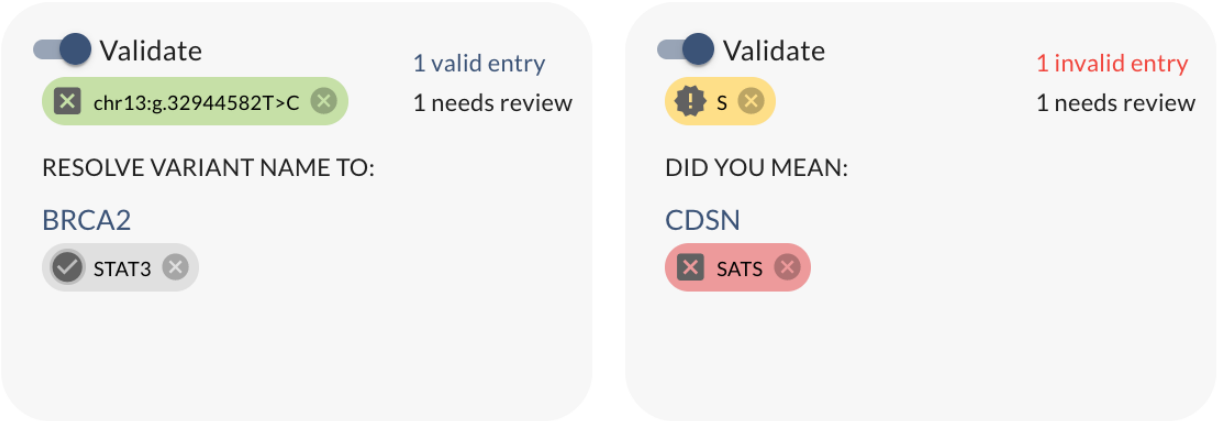


Fig. S1 Gene Names Validation. SigCom LINCS validates user-inputted gene names against all the gene names registered in the SigCom LINCS metadata. The validation function provides an option for users to resolve synonymous IDs and gene names that do not have an exact match with the registered name. This function facilitates harmonization of the input sets with the gene metadata within SigCom LINCS.

Fig. S2

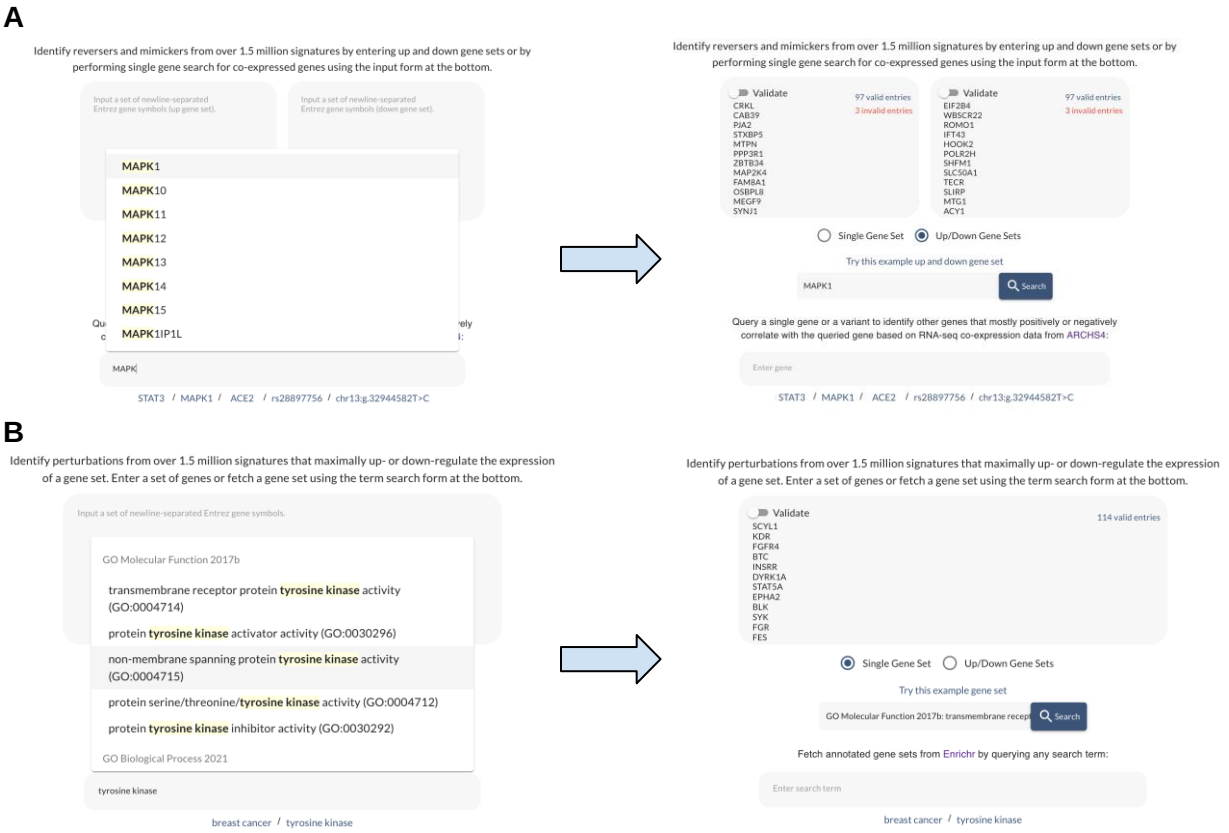


Fig. S2 Fetching signature search on co-expression and Enrichr gene sets. SigCom LINCS can retrieve gene sets from other resources by (A) converting a single gene or a variant to up and down gene sets using ARCHS4 co-expression data, and (B) fetching Enrichr gene sets via its search term search API.

Fig. S3

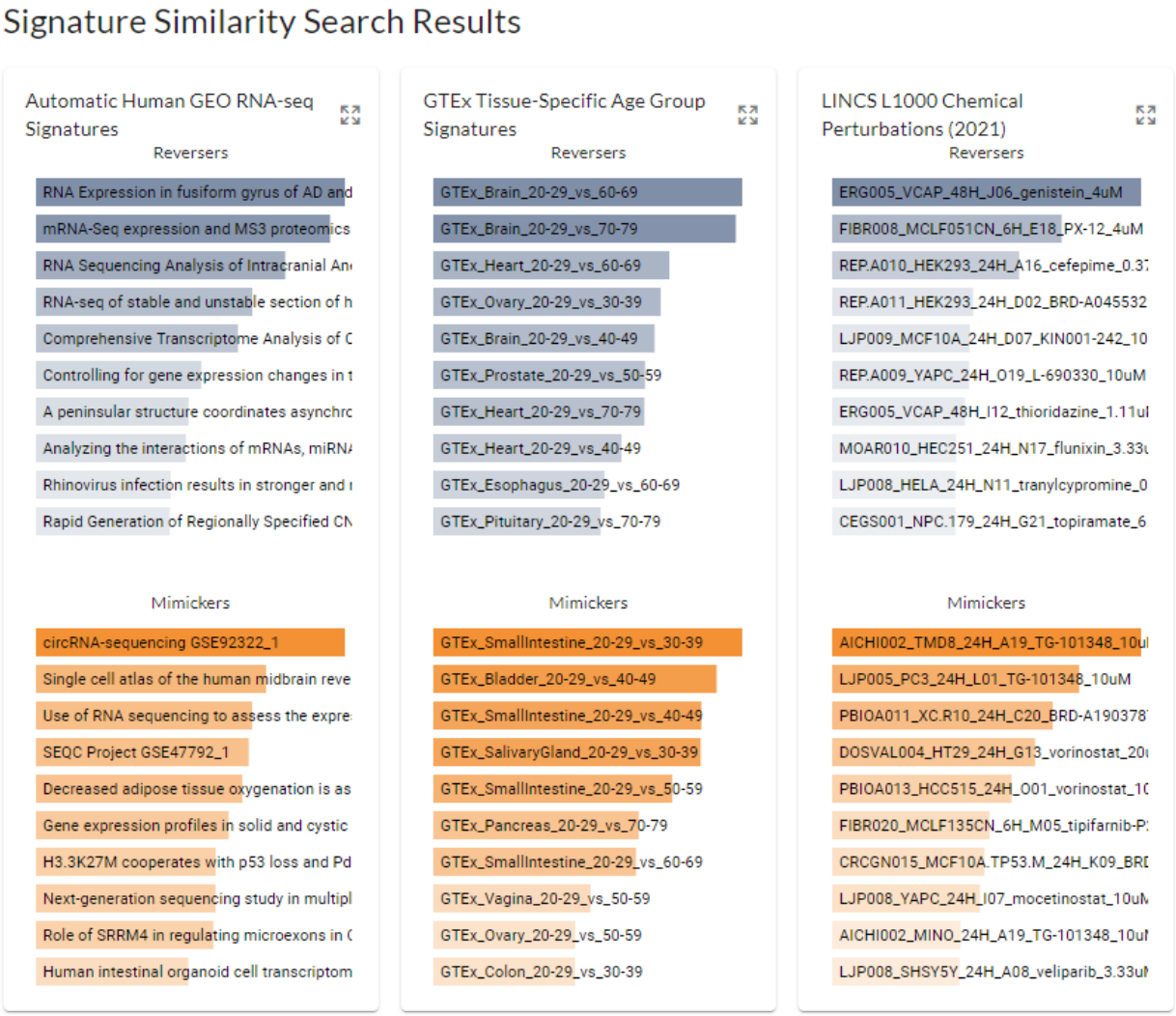


Fig. S3 SigCom LINCS search results overview. Once the user presses submit, the initial results page displays bar charts for each collection of signatures.

Fig. S4

Reversers

FILTERS EXPORT TABLE EXPORT GENE RANK MATRIX

Perturb...	Dose	Tissue	Cell Line	Timepoi...	log p-val...	log p-val...	z-score (...	p-value ...
genistein	4 uM	prostate gland	VCAP	48 h	31.21	12.87	-10.39	1
PX-12	4 uM		MCLF051CN	6 h	26.34	12.34	-9.509	1
cefepime	0.37 uM	kidney	HEK293	24 h	25.00	8.298	-9.036	1.9386e-2
BRD-A04553...	3.33 uM	kidney	HEK293	24 h	21.69	10.21	-8.525	1
KIN001-242	10 uM	breast	MCF10A	24 h	21.66	9.392	-8.486	1
L-690330	10 uM	pancreas	YAPC	24 h	21.46	10.29	-8.478	1
thioridazine	1.11 uM	prostate gland	VCAP	48 h	21.23	10.36	-8.433	1
flunixin	3.33 uM	endometrium	HEC251	24 h	21.00	9.077	-8.337	1
tranylcypromi...	0.12 uM	uterine cervix	HELA	24 h	20.88	9.427	-8.327	1

Mimickers

FILTERS EXPORT TABLE EXPORT GENE RANK MATRIX

Perturb...	Dose	Tissue	Cell Line	Timepoi...	log p-val...	log p-val...	z-score (...	p-value ...
TG-101348	10 uM	lymphoid syst...	TMD8	24 h	28.28	13.78	9.905	1
TG-101348	10 uM	prostate gland	PC3	24 h	25.60	12.56	9.371	1
BRD-A19037...	10 uM	epithelium	XC.R10	24 h	25.52	8.489	9.145	1
vorinostat	20 uM	intestine	HT29	24 h	24.38	9.107	8.993	8.0642e-2
vorinostat	10 uM	lung	HCC515	24 h	23.41	8.782	8.789	1.5429e-1
tipifarnib-P2	4 uM		MCLF135CN	6 h	21.96	10.95	8.601	1
BRD-A19037...	1.11 uM	breast	MCF10A	24 h	22.32	8.401	8.556	1
mocetinostat	10 uM	pancreas	YAPC	24 h	25.14	4.612	8.518	4.2123e-4
TG-101348	10 uM	blood	MINO	24 h	20.99	9.455	8.352	1

Fig. S4 Tabular view of the top signatures. Tabular views of the top signatures are provided for users to inspect the metadata and scores of the results. These tables are downloadable and are provided to the users in TSV format.

Fig. S5

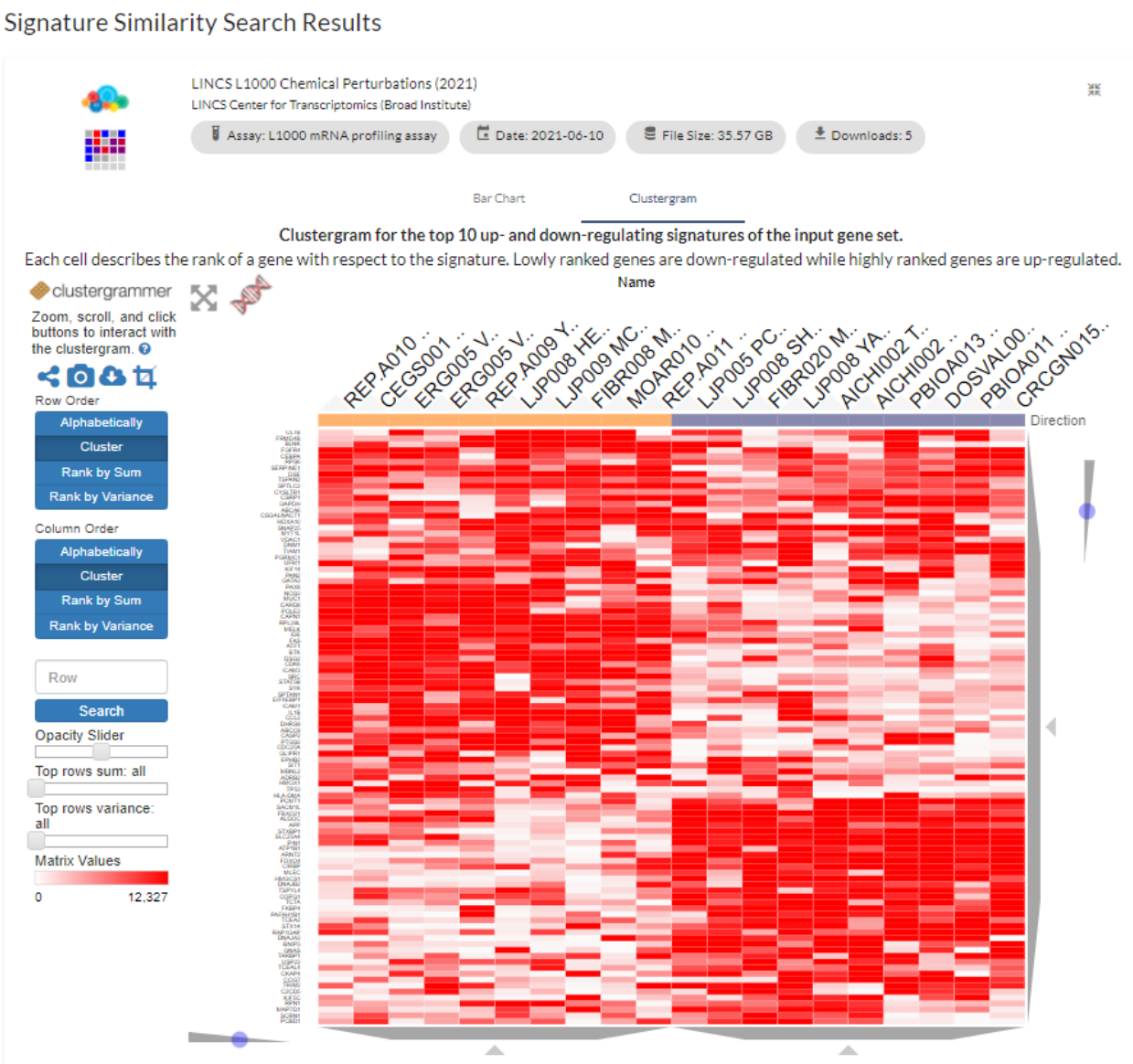


Fig. S5 Interactive heatmap of the top mimickers and reversers. The heatmap visualizes the ranks of the overlapping genes with the top up and down matching signatures. A high matrix value represents a high rank. The figure is interactive, enabling zooming, panning, sorting, clustering, and filtering.

Fig. S6

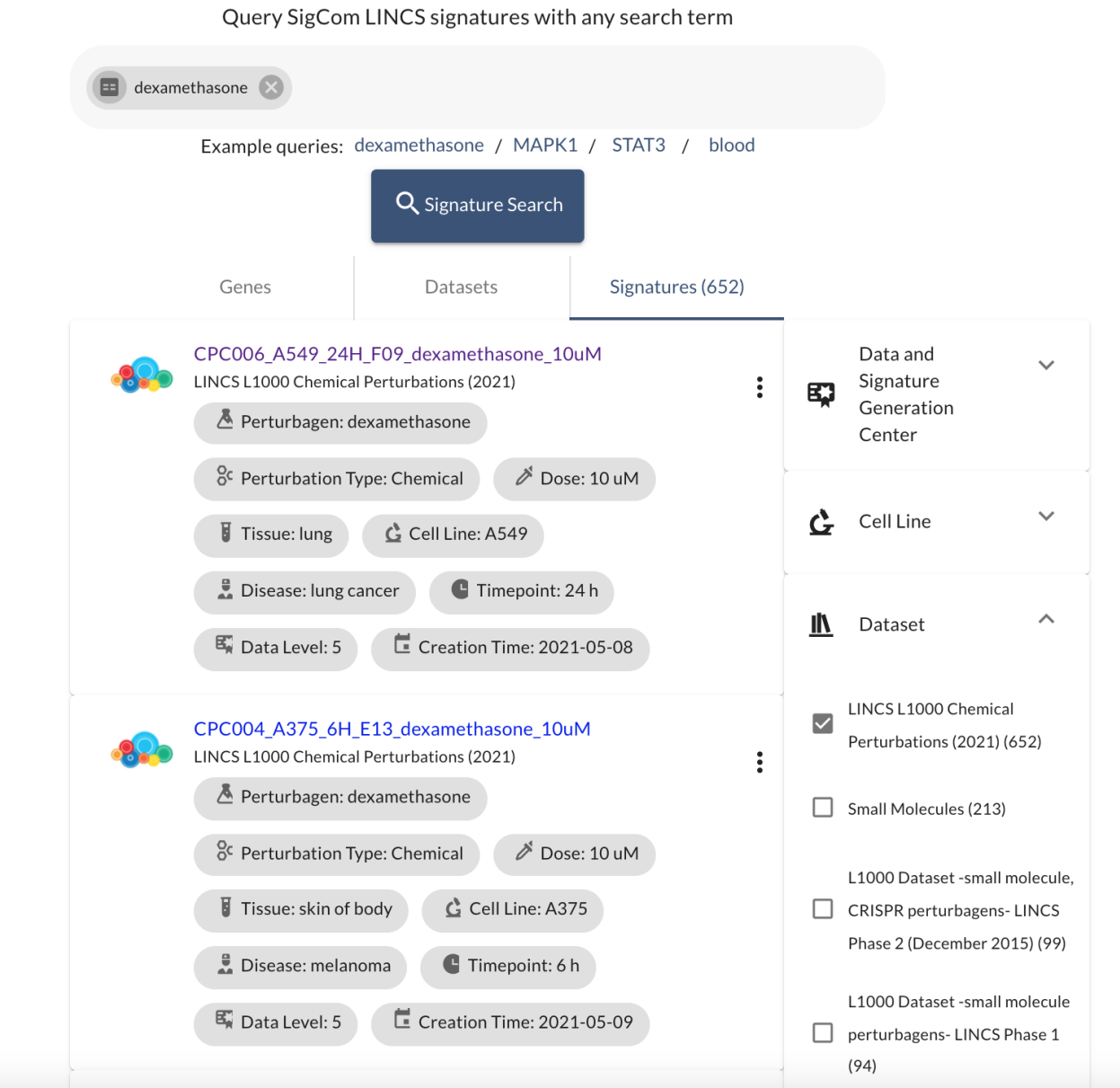


Fig. S6 Metadata search results. The SigCom LINCS metadata search interface enables users to query the SigCom LINCS database for retrieving signatures using any search term, for example, a cell line, a drug, or a gene. Once the search is complete, filters can be used to narrow down the search.

Fig. S7

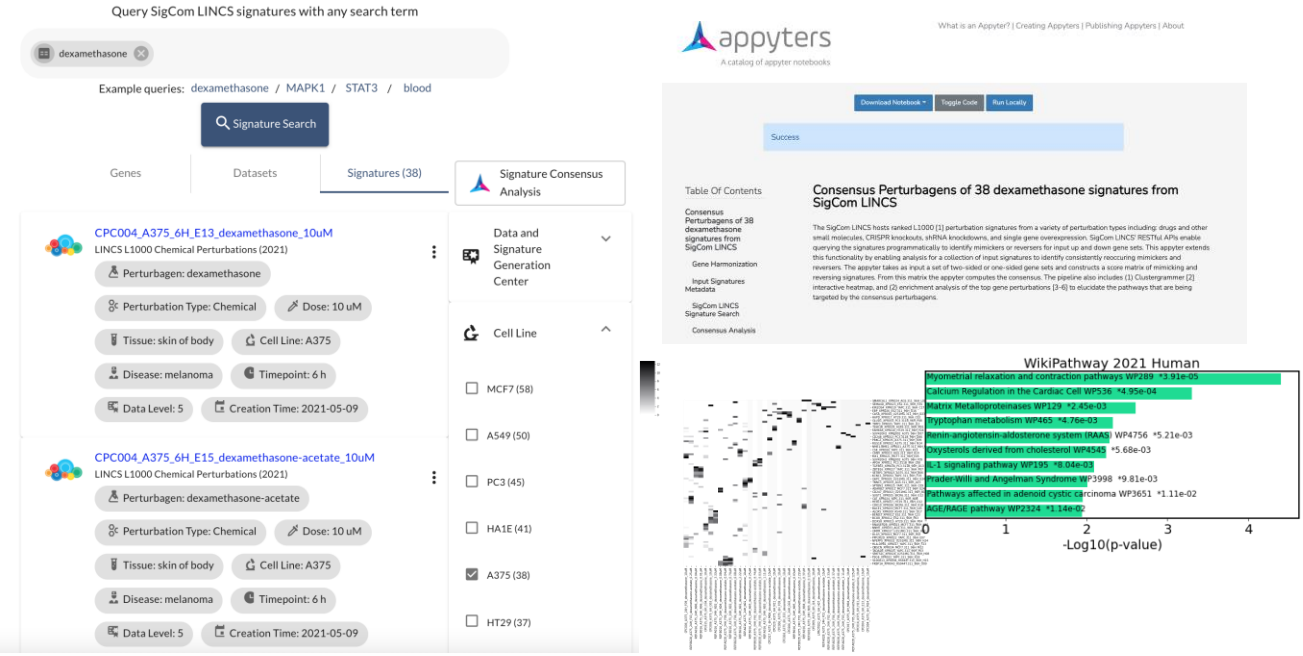


Fig. S7 Consensus analysis. SigCom LINCS provides an option to perform consensus analysis for a collection of signatures within the SigCom LINCS database. Metadata search queries that return less than 50 signature can be piped for analysis with the Signature Consensus Appyter. The SigCom LINCS Consensus Appyter produced a report that provides insights about the common mimickers and reversers across the collection of input signatures.

Fig. S8

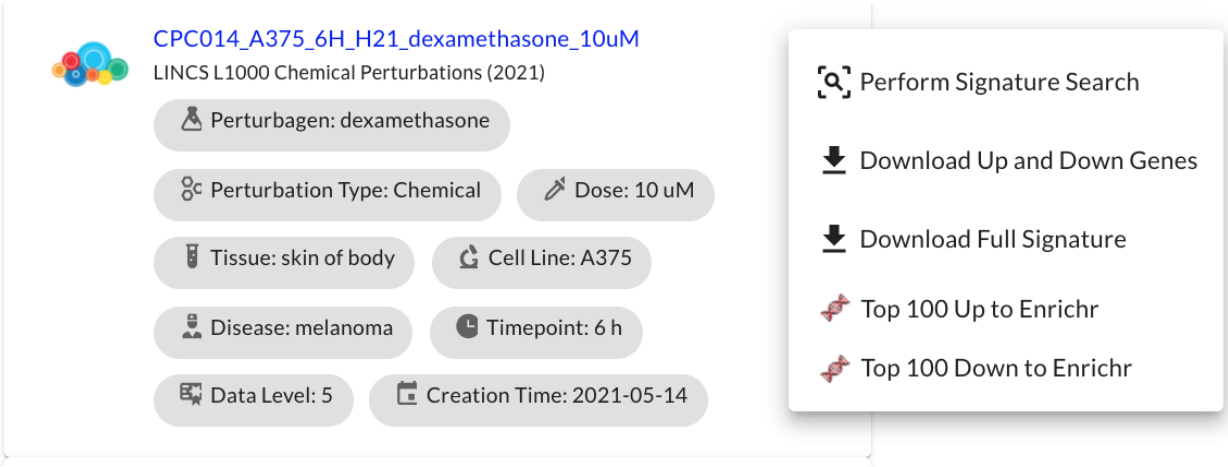


Fig. S8 Accessing signature data. Individual signatures can be downloaded as a JSON file or a GMT file that contain the up and down gene sets for the signature. Users can also use the signature data for SigCom LINCS signature search. Furthermore, the up or down gene sets can be sent to Enrichr for enrichment analysis.

Fig. S9

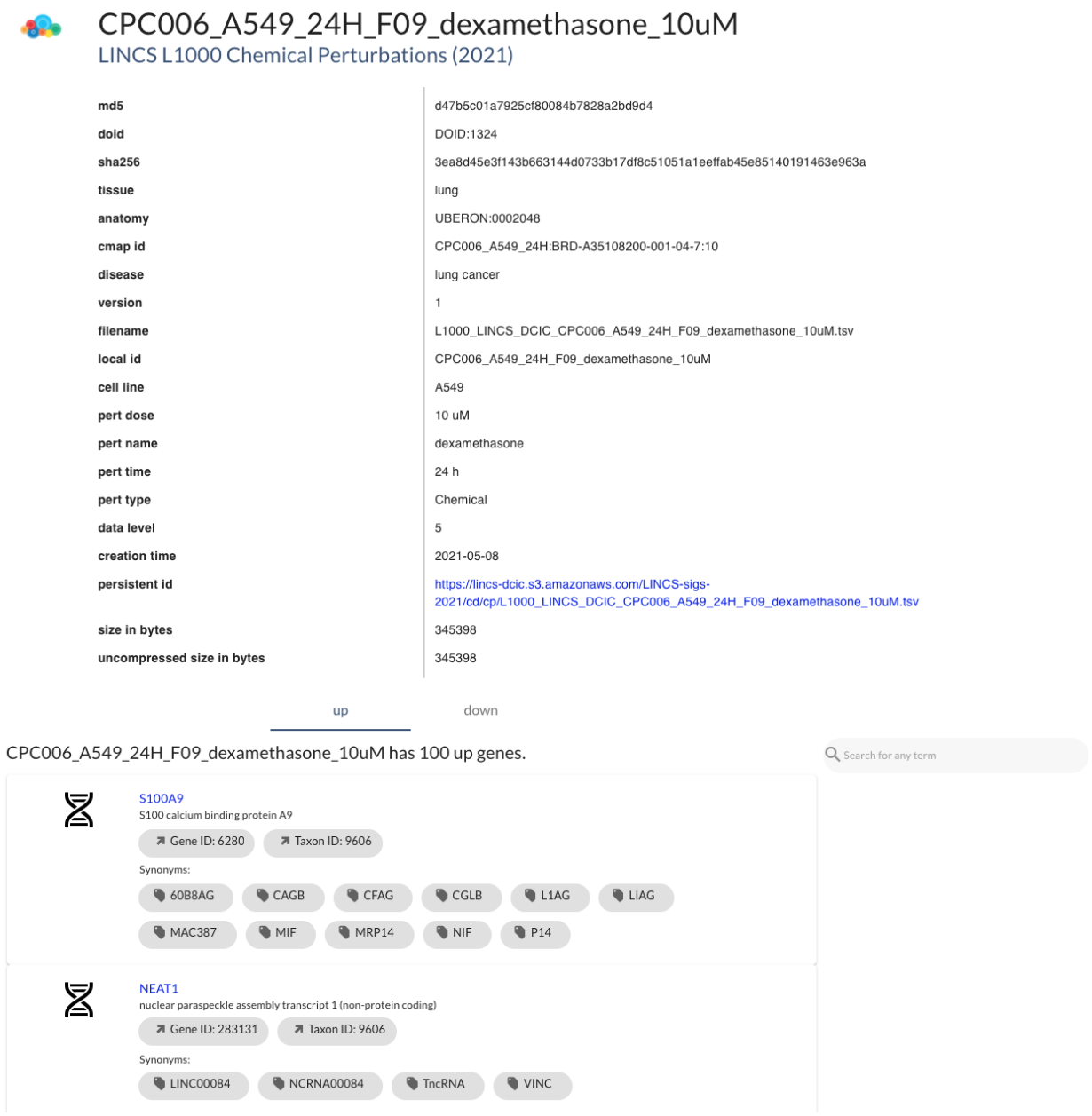
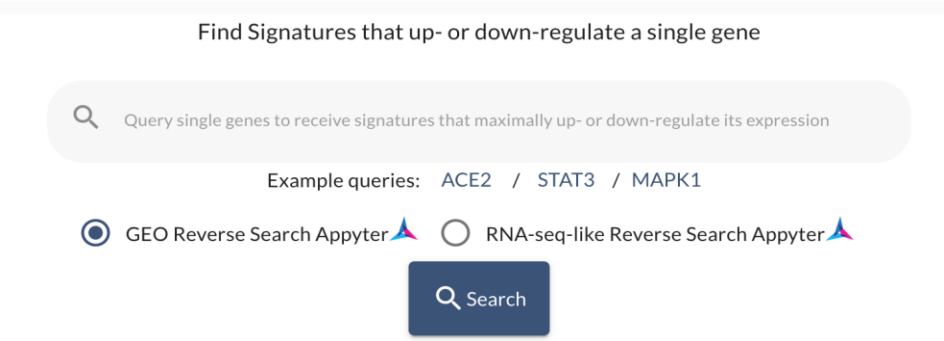


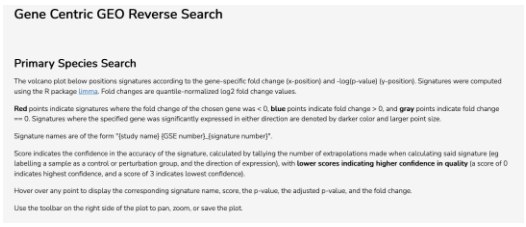
Fig. S9 Metadata pages Clicking on metadata search results opens the metadata landing page which features the expanded metadata of the entry.

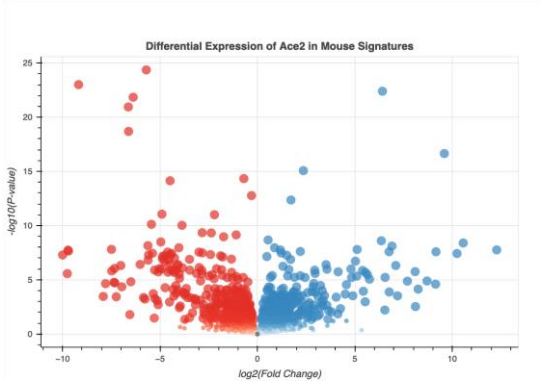
Fig. S10

A.

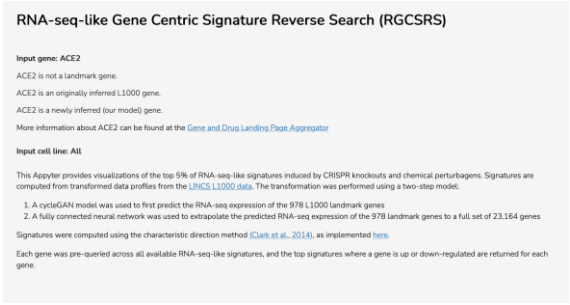


B.





C.



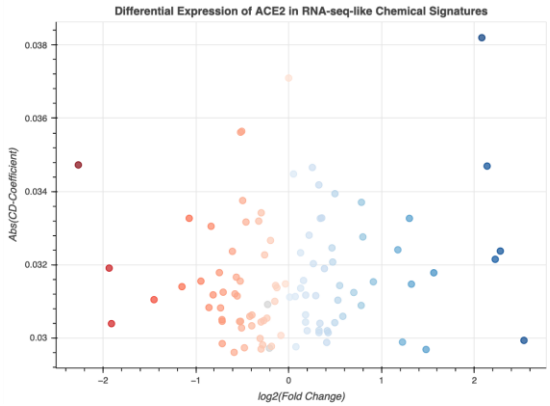


Fig. S10 Single gene reverse search Appyters A) The SigCom LINCS gene search page can be used to perform reverse signature search for a single human gene. The search identifies signatures that maximally up- or down-regulate the gene. Performing a gene search redirects the users to one of two Appyters. B) The identified automated GEO signatures, and C) the RNA-seq-like signatures from L1000 signatures are visualized as volcano plots.

Fig. S11

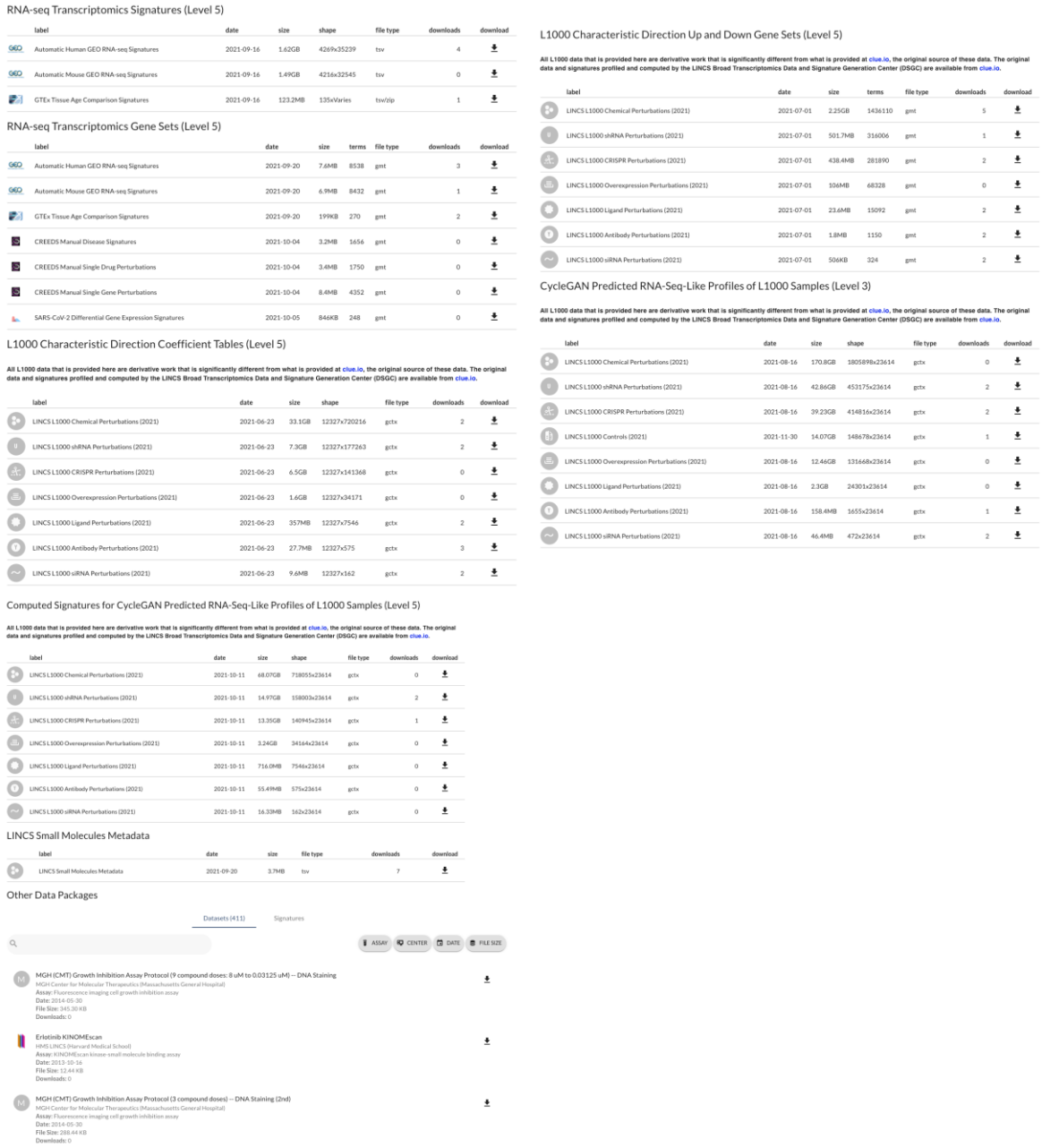


Fig. S11 The SigCom LINCS download page. All links to the Level 5 full signatures data, Level 3 expression profiles, as well as GMT files of the up and down gene sets are accessible on the download page. Users are also provided links to the predicted RNA-seq-like profiles from L1000 samples as well as legacy LINCS datasets from the original LINCS data portal.

Fig. S12

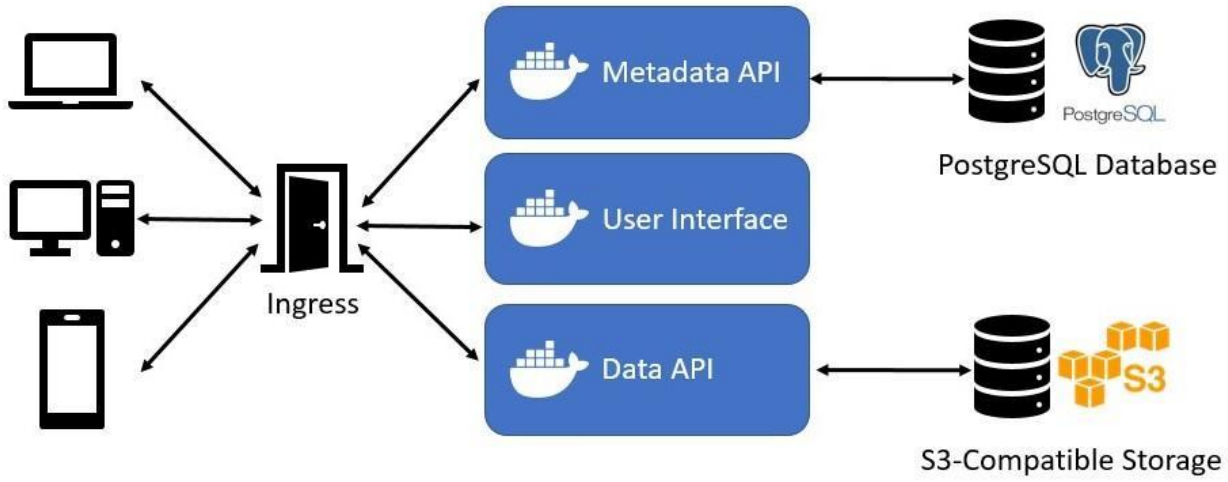


Fig. S12 The Signature Commons architecture. Signature Commons is composed of three microservices that are containerized with Docker. The SigCom LINCS repository provides images for ingress, as well as PostgreSQL and S3 storage. These are replaceable with services offered by cloud providers.

Fig. S13

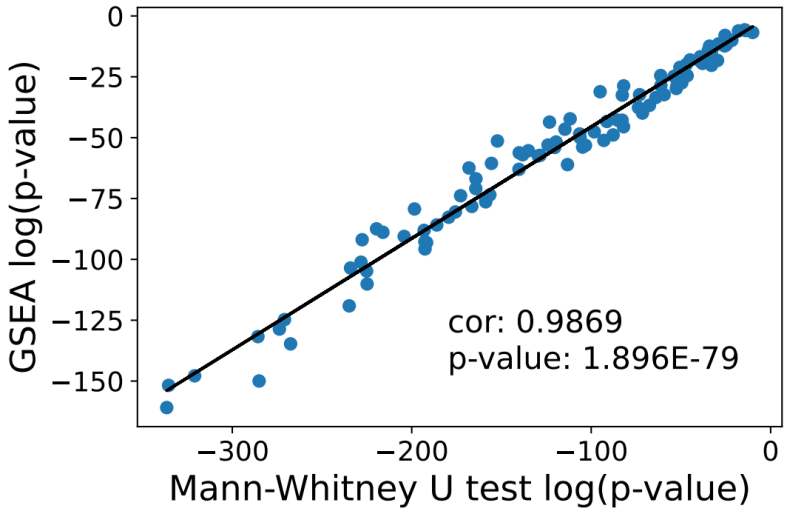


Fig. S13 Comparing the MWU test with the GSEA test. P-values produced by MWU and blitzGSEA for 100 gene sets with varying degrees of significance. To generate the random gene set ranks, we uniformly sample random rank positions in ranges of the full rank for different sizes of gene sets.

Fig. 14

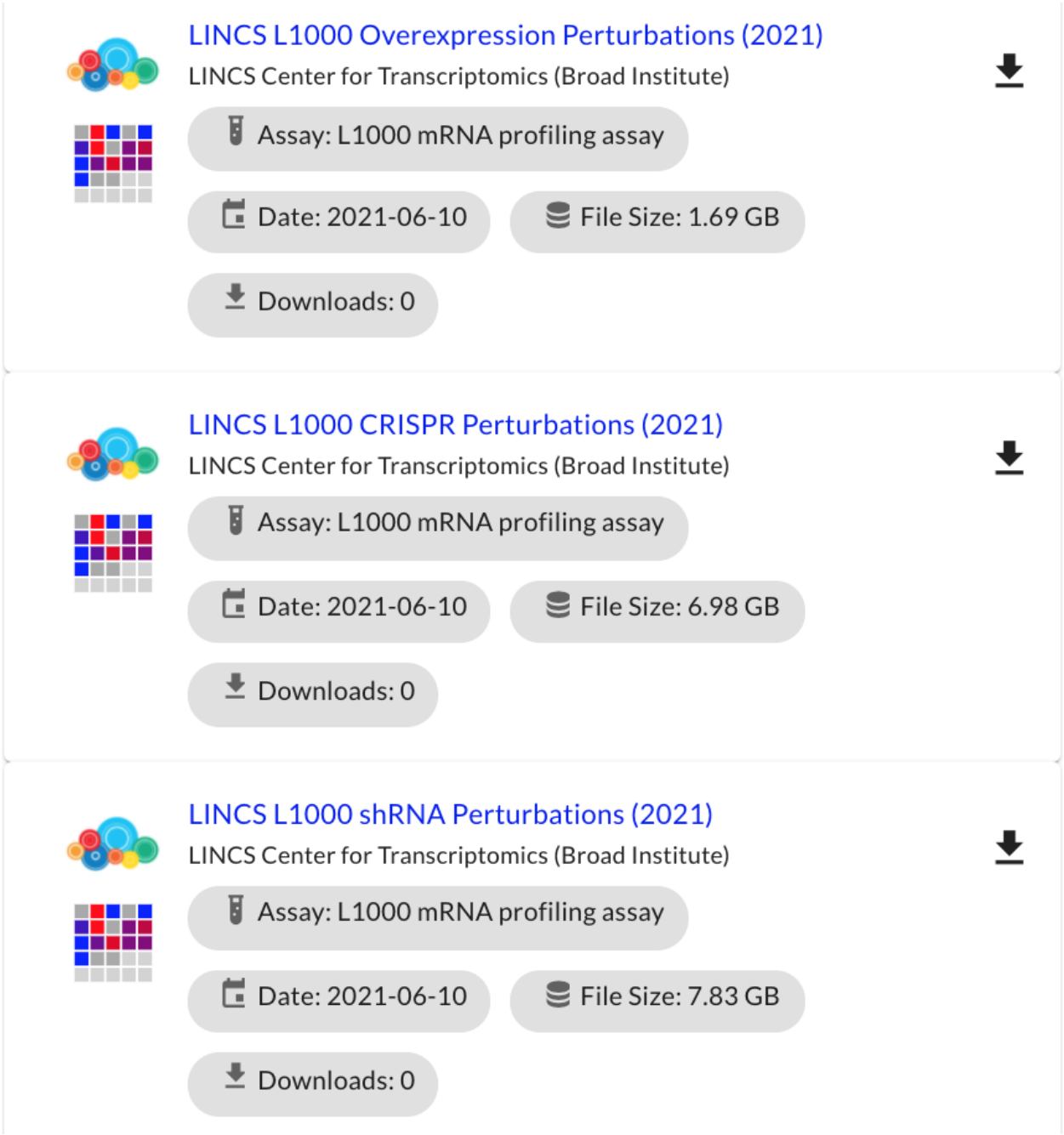


Fig. S14 FAIR Assessments of the datasets and signatures within SigCom LINCS. The datasets and signatures in SigCom LINCS were assessed for FAIRness with FAIRshake with a unique rubric. These assessments are displayed near each dataset and signature entry as the FAIRshake insignia. Each square in the insignia represents a FAIR metric which asserts the adherence of the dataset and signature to the FAIR guiding principles.

SUPPORTING TABLES

Table S1

dataset	Signatures	Perturbations (drugs, genes, diseases, age groups)	Tissues of origin	Cell lines
LINCS L1000 Chemical Perturbations	718055	28564	34	196
LINCS L1000 shRNA Perturbations	158003	4917	15	22
LINCS L1000 CRISPR Perturbations	140945	5157	18	27
LINCS L1000 Overexpression Perturbations	34164	4040	10	20
LINCS L1000 Ligand Perturbations	7546	329	8	15
Automatic Human GEO RNA-seq Signatures	4269	-	-	-
Automatic Mouse GEO RNA-seq Signatures	4216	-	-	-
CREEDS Manual Single Gene Perturbations	2176	870	1364	-
CREEDS Manual Single Drug Perturbations	875	271	648	-
CREEDS Manual Disease Signatures	828	333	501	-
LINCS L1000 Antibody Perturbations	575	4	8	12
LINCS L1000 siRNA Perturbations	162	23	1	1
GTEx Aging Signatures	135	5	28	-

Table S1. Signature types in SigCom LINCS. SigCom LINCS catalogs over one million gene expression signatures along with their metadata generated from LINCS L1000 data, cDNA microarrays and RNA-seq from GEO, and RNA-seq data from GTEx.

Table S2

Label	Frequency	Category	num_gse
rep	23641	0	1733
rna	16840	0	2040
seq	13681	0	1829
replicate	6047	0	465
control	6023	1	1212
sample	5762	0	266
rnaseq	4654	0	363
patient	4557	0	173
cd	4244	0	261
cells	4094	0	395
dmso	3885	1	632
hr	3318	0	158
day	3317	0	180
wt	3081	1	619
tissue	3064	0	50
lib	2744	0	16
from	2727	0	1059
post	2677	2	59
donor	2642	0	159
+	2389	0	268
with	2115	0	169
mcf	2029	0	223
treated	2013	2	247
hra	1943	0	4
cgnd	1942	0	3
ctrl	1939	1	351
ko	1935	2	314
enclb	1858	0	983
shrna	1751	2	625
mortem	1706	0	1
seqc	1692	0	2

ilm	1691	0	1
mrna	1642	0	177
tumor	1629	2	91
x	1553	0	97
blood	1512	0	40
fgc	1358	0	2
fcc	1349	0	3
nm	1311	0	101
human	1305	0	135
non	1279	0	121
cell	1260	0	198
sirna	1259	2	220
il	1243	0	100
ad	1234	0	61
tr	1209	0	26
healthy	1197	1	84
vumc	1169	0	3
tb	1165	0	18
week	1152	0	21
hd	1119	0	36
acxx	1111	0	5
treatment	1090	2	80
total	1083	0	320
kd	1074	2	209
subject	1064	0	29
lb	1059	0	10
mc	1013	0	17
of	1008	0	116
ms	1000	0	31
clone	995	0	92
hek	978	0	94
ac	902	0	31
platelets	899	0	5
untreated	891	1	176
na	889	0	13
pre	888	0	57
mock	887	1	191

hepg	877	0	323
sh	877	0	135
individual	867	0	16
gfp	865	0	132
um	849	0	93
in	846	0	83
dox	820	2	111
w	818	0	76
vehicle	782	1	138
exp	781	0	43
biological	765	0	59
normal	764	1	107
mda	751	0	104
line	748	0	76
subjects	748	0	2
mb	747	0	105
bd	745	0	13
pc	737	0	95
hcc	732	0	71
mp	731	0	9
ir	719	0	18
hela	716	0	107
at	716	0	41
aml	707	0	33
lncap	690	0	79
pf	667	0	17
case	662	2	19
baseline	661	1	25
ipsc	658	0	71
no	642	0	89
lps	638	2	69
pt	635	0	52
for	632	0	81
nt	619	0	105
male	615	0	26
primary	614	0	51
hours	604	0	42

af	594	0	34
batch	593	0	36
lung	589	0	55
cb	586	0	45
hc	579	0	48
hct	578	0	85
su	570	0	30
progressor	567	0	3
liver	562	0	49
pbmc	560	0	34
biopsy	555	0	14
jq	547	0	69
hrs	545	0	41
time	542	0	18
mir	533	0	83
cancer	533	0	36
infected	527	2	72
fgf	519	2	7
con	515	1	86
hs	513	0	58
gbm	509	0	22
risk	509	0	3
si	504	0	78
bc	492	0	27
plus	490	0	66
us	489	0	15
disease	484	2	18
female	482	0	25
nc	474	0	127
knockdown	473	2	84
subjectsle	468	0	1
high	461	0	68
sl	458	0	12
eu	457	0	6
polya	456	0	98
ctl	456	1	64
mm	454	0	53

vector	449	1	121
oe	444	2	70
naïve	441	1	20
fgfr	432	0	3
parental	429	0	84
neg	424	1	76
pd	422	0	48
sam	419	0	15
sle	414	0	15
tn	413	0	8
dm	412	0	39
npc	412	0	37
ba	411	0	21
molm	404	0	37
cn	403	0	9
ln	402	0	31
veh	397	1	78
repl	397	0	26
ns	395	0	47
ra	394	0	42
low	393	1	68
hesc	393	0	53
sw	389	0	53
mut	382	2	44
patients	377	0	5
re	372	0	27
lane	370	0	7
gm	368	0	45
after	366	2	26
uc	361	0	17
tdimi	361	0	1
ips	359	0	37
yri	359	0	1
panc	356	0	40
pos	355	0	46
and	352	0	70
uninfected	349	1	39

mv	349	0	33
transfected	345	2	33
ls	344	0	22
bgi	342	0	3
imr	339	0	43
fc	339	0	15
fibroblasts	338	0	35
ex	338	0	24
pa	335	0	25
fulv	335	0	3
cajmranxx	335	0	2
crohn's	334	0	7
bt	333	0	52
on	333	0	31
nsclc	333	0	6
dx	331	2	4
repeat	330	0	40
th	325	0	24
whole	322	0	18
may	322	0	2
naive	320	1	46
days	319	0	30
ni	319	0	16
msc	318	0	38
bulk	316	0	26
thp	312	0	51
vu	311	0	5
ht	308	0	51
rv	306	0	45
mg	304	0	40
os	303	0	44
empty	301	0	73
sictrl	301	1	68
sum	301	1	29
cnl	301	1	2
pbmcs	299	0	14
cohort	295	0	3

tet	293	0	31
aid	290	0	18
kidney	289	0	27
anxx	289	0	5
pdac	289	0	2
min	287	0	35
ct	287	1	34
sicontrol	286	1	66
etoh	286	0	42
pat	286	0	8
sc	285	1	41
prostate	285	0	13
ca	283	0	34
sk	282	0	50
palbo	281	0	4
colon	280	0	31
tgfb	278	0	35
type	277	0	62
jc	276	0	4
jia	274	0	5
cgga	274	0	1
technical	270	0	12
derived	269	0	33
negative	268	1	57
mo	268	0	16
jacxx	268	0	3
ctr	267	1	47
pdx	267	0	28
wild	265	1	60
fg	262	0	4
nvs	262	0	2
input	260	0	52
gsk	259	0	38
rpe	259	0	36
stimulated	257	2	26
old	257	0	21
fibroblast	256	0	45

agr	256	0	1
hypoxia	255	0	43
muscle	255	0	26
st	255	0	26
rseq	255	0	2
huvec	252	0	44
fetal	251	0	25
tgf	251	0	22
rs	251	0	21
crpc	250	0	4
tnf	249	0	33
lv	249	0	17
tu	248	0	9
ev	247	0	70
cc	247	0	29
up	247	0	5
scc	246	0	24
mk	246	0	18
hiv	245	0	17
sgrna	244	0	24
young	243	0	23
controls	243	1	4
fiin	241	0	1
ifn	239	0	33
nuclear	239	0	24
dgm	239	0	11
cr	238	0	31
znf	237	0	18
resistant	236	2	42
ttr	236	0	3
copd	236	0	2
cm	235	0	42
nd	233	0	27
dld	231	0	20
macrophages	231	0	17
dht	230	0	35
skin	229	0	37

du	228	0	26
wm	227	0	23
br	226	0	18
ut	225	0	35
jurkat	224	0	31
analyzed	224	0	8
diff	222	0	22
hi	220	0	22
crispri	219	0	82
pb	218	0	21
overexpressed	218	2	13
ec	217	0	33
sp	216	0	31
mutant	213	2	35
dc	211	0	36
bm	211	0	35
id	211	0	13
ab	210	0	25
cl	210	0	24
tatagcct	210	0	1
mrnaseq	209	0	19
ggctctga	209	0	1
nl	208	0	15
analysis	208	0	12
atagaggc	208	0	1
hipsc	206	0	18
al	206	0	8
poly	204	0	37
to	204	0	19
gy	204	0	17
nasal	204	0	7
point	203	0	5
moi	202	0	10
sn	202	0	6
meningioma	202	0	2
paxgeneday	202	0	1
µm	201	0	15

fd	201	0	12
infection	200	2	15
ml	199	0	31
hour	199	0	16
ileal	199	0	1
ribo	198	0	17
group	198	0	11
differentiation	197	0	12
arthritis	197	0	3
rectal	197	0	2
globin	197	0	1
block	197	0	1
minus	195	0	30
msi	195	0	7
cctatcct	195	0	1
pbs	194	0	38
tc	194	0	18
bx	193	0	7
ng	192	1	22
brain	191	0	34
sb	191	0	21
tm	191	0	17
scramble	190	1	47
egf	190	0	20
rheumatoid	190	0	2
cytoplasmic	189	0	14
sm	188	0	13
amc	188	0	4
huh	185	0	33
ar	185	0	27
fnanxx	185	0	2
shctrl	184	1	48
sa	184	0	33
follow	184	0	1
hap	183	0	13
hf	183	0	13
hmec	183	0	7

tpm	183	0	2
experiment	182	0	18
dlpfc	182	0	4
hl	180	0	27
mt	180	2	23
participant	180	0	2
cnhi	180	0	1
sr	179	0	22
transduced	179	2	18
hfanxx	179	0	2
adult	178	0	32
rh	178	0	21
la	178	0	20
vcap	177	0	19
es	176	0	28
lm	176	0	25
rp	176	0	18
hpi	175	0	16
ov	175	0	12
ta	175	0	11
leicester	175	0	1
longitudinal	175	0	1
cs	174	0	22
timepoint	174	0	5
nk	173	0	25
xenograft	173	0	13
aza	172	0	24
as	171	0	29
sf	171	0	24
htert	171	0	19
monocyte	171	0	16
zt	171	0	2
knockout	170	2	31
set	170	0	16
bj	169	0	28
nb	169	0	27
unstimulated	169	1	27

co	167	0	29
all	167	0	20
bs	167	0	7
wb	167	0	4
only	166	0	17
msn	166	0	2
adipose	165	0	17
run	165	0	7
validation	165	0	4
gs	164	0	8
rpmi	163	0	25
arid	163	0	19
culture	162	0	17
stim	162	0	11
nutlin	161	2	21
ovcar	161	0	19
scr	160	1	38
ifng	160	2	21
discovery	160	0	2
uacxx	160	0	1
aypacxx	160	0	1
aytacxx	160	0	1
neuron	159	0	18
bl	159	0	9
year	158	0	5
normoxia	157	0	27
neurons	157	0	12
nsc	156	0	29
hep	155	0	32
yap	155	0	23
targeting	154	0	28
mel	154	0	26
obese	154	0	8
mdamb	153	0	18
hfwb	153	0	1
gr	152	0	11
sub	152	0	10

stem	151	0	22
fb	151	0	19
kras	151	0	10
mgh	151	0	5
nki	151	0	2
gdanxx	151	0	1
norm	150	1	9
lesional	150	0	3
expression	149	0	10
lc	149	0	10
epithelial	148	0	22
ociaml	148	0	9
heart	147	0	27
alpha	147	0	17
bone	147	0	17
auxin	147	0	15
epi	147	0	11
dose	147	0	6
acp	147	0	4
ha	146	0	24
lu	146	0	9
diagnosis	145	0	4
cll	144	0	13
endo	144	0	11
combo	142	0	23
differentiated	141	2	21
tgacca	141	0	20
cf	141	0	20
cgatgt	141	0	17
cg	141	0	5
study	141	0	5
lh	141	0	5
bp	140	0	20
condition	140	0	11
dt	140	0	9
cagatc	139	0	18
ly	138	0	24

dex	138	2	22
acagtg	138	0	17
yr	138	0	5
cttgta	137	0	18
gccaat	137	0	17
undiff	137	1	14
dn	136	0	18
hmsc	136	0	11
covid	136	0	9
oci	135	0	16
dcas	135	0	13
colorectal	135	0	4
lab	135	0	4
pool	134	0	18
aggcgaag	134	0	1
zzz	133	0	68
virus	133	0	15
stimulation	133	2	6
sequencing	133	0	4
hokt	133	0	2
wildtype	132	1	29
null	132	1	25
positive	132	2	23
pr	132	0	19
serum	132	0	17
atcacg	132	0	16
miapaca	132	0	16
tp	132	0	16
cutll	132	0	15
peripheral	132	0	12

Table S2 List of frequent terms identified in sample labels of GEO GSMs

Feature	SigCom LINCS	L1000 FWD	clue.io	iLINCS	L1000 CDS2	LDP1	LD2	LINCS Canvas Browser
2021 Release	X		X					
Access Indv. Sigs.	X	X		X	X		X	
Sig. Search	X	X	X	X	X		X	X
# of Sigs.	~1M	~16K	~1M	~200K	~20K	N/A	~500K	~100K
Ontology Metadata	X			X		X	X	
Gene Pages	X							
Drug Pages		X	X				X	
Metadata Search	X	X	X	X		X	X	
Gene to Sigs.	X							
Terms to Sig.	X							
Open API	X	X	X	X		X	X	
Regist. Required			X					
Heat maps	X		X		X			X
UMAP PCA t-SNE	X	X						

Table S3. Comparison of SigCom LINCS to other tools serving LINCS data and signatures.