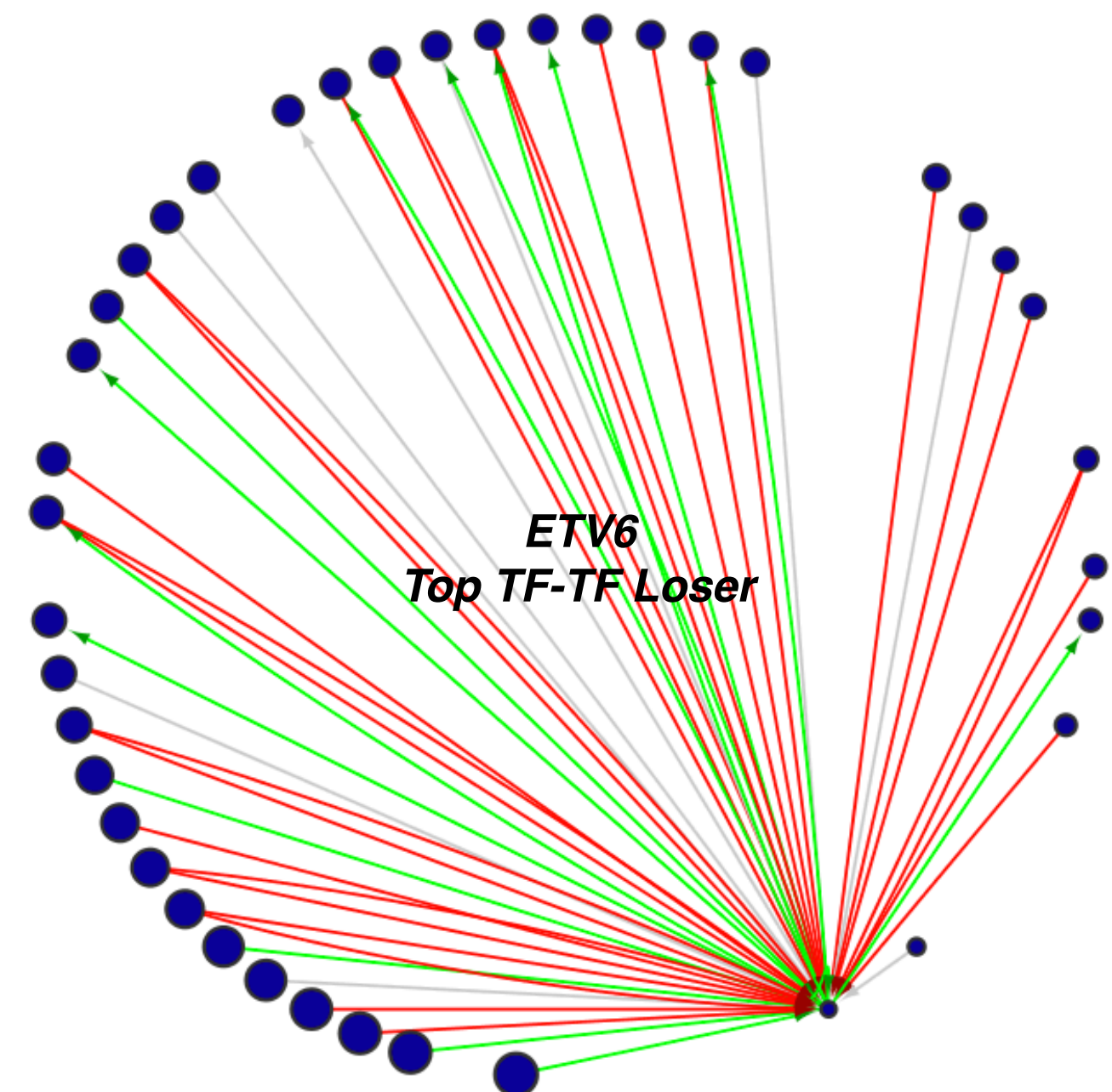
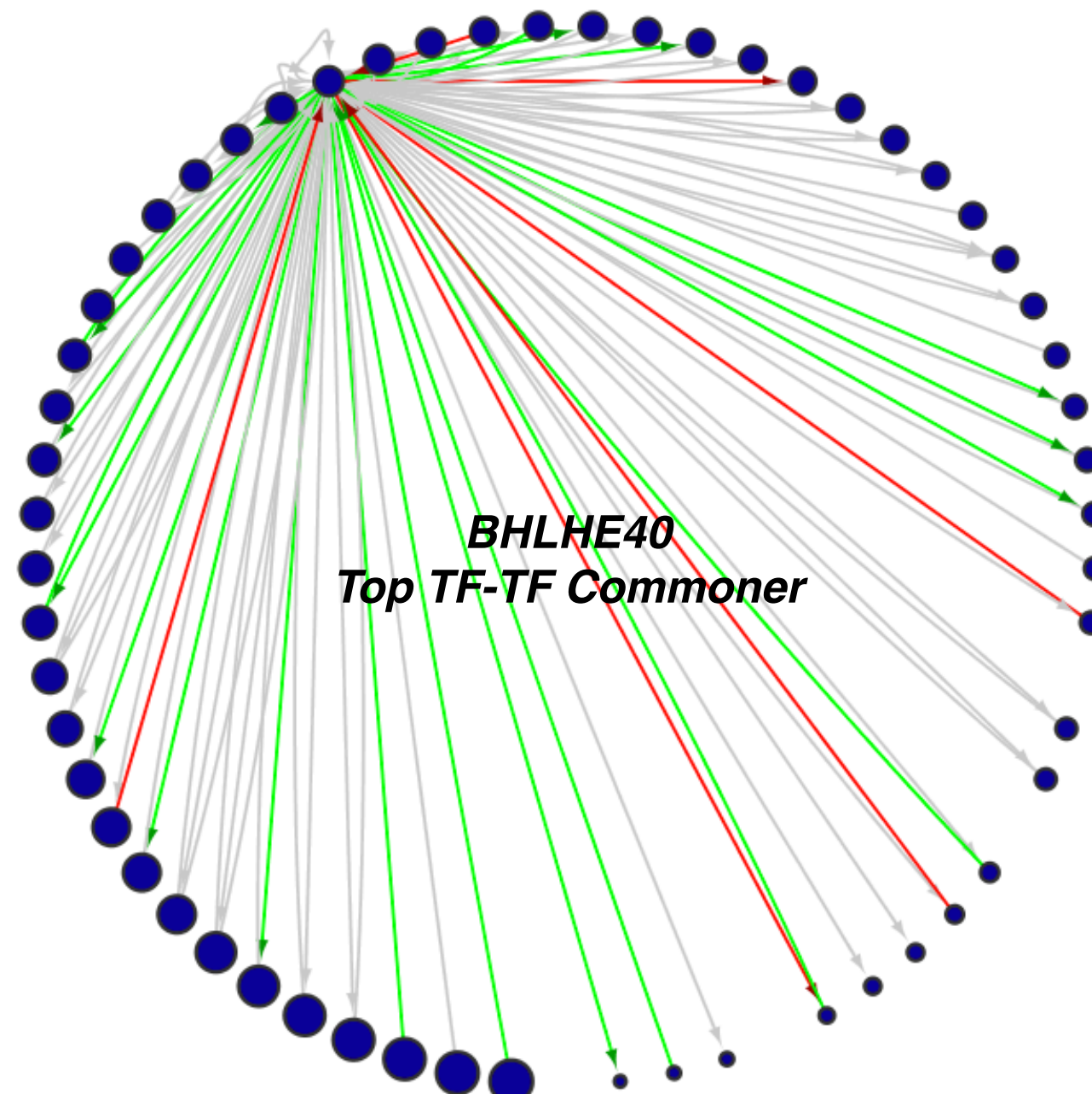
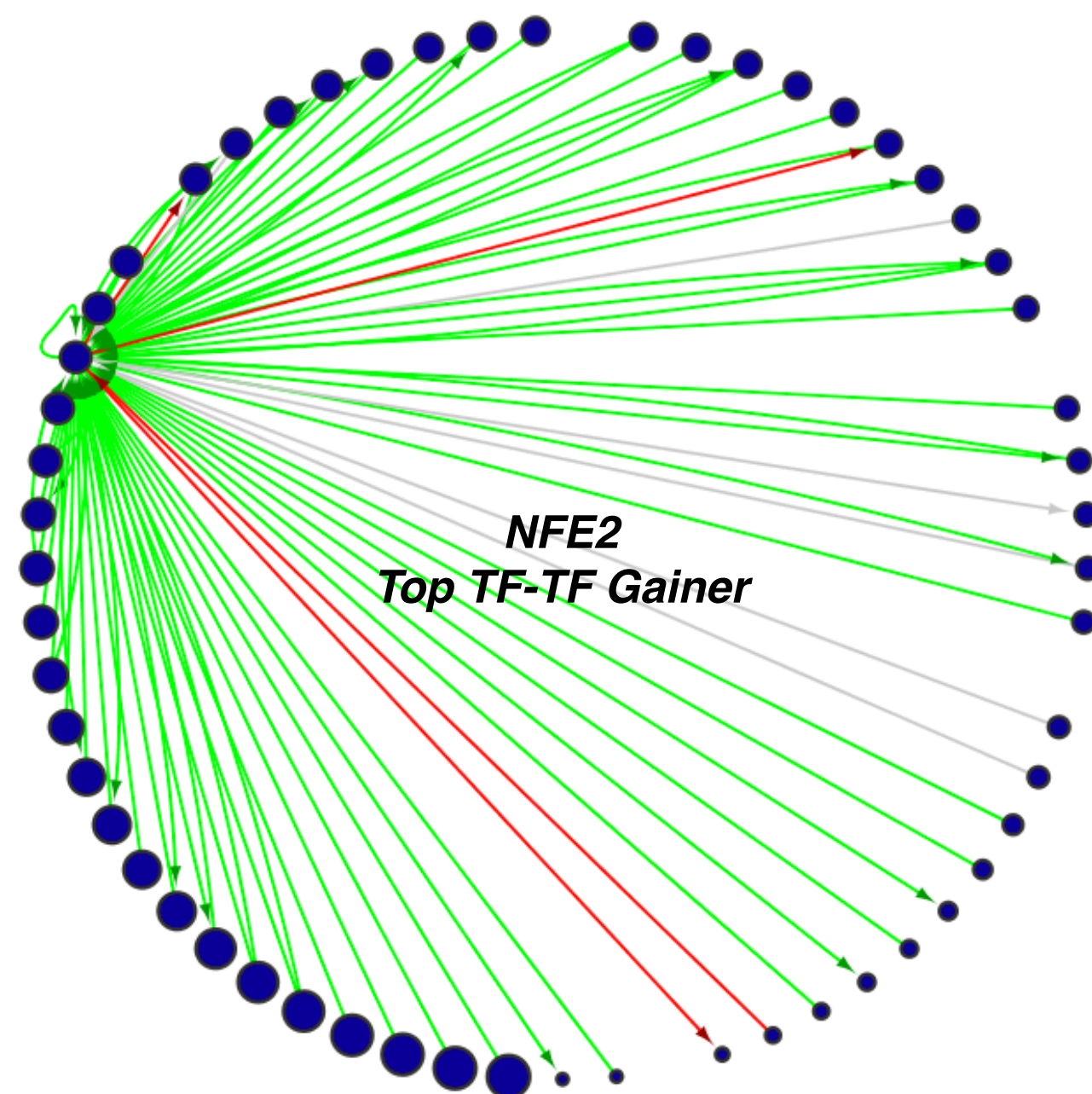
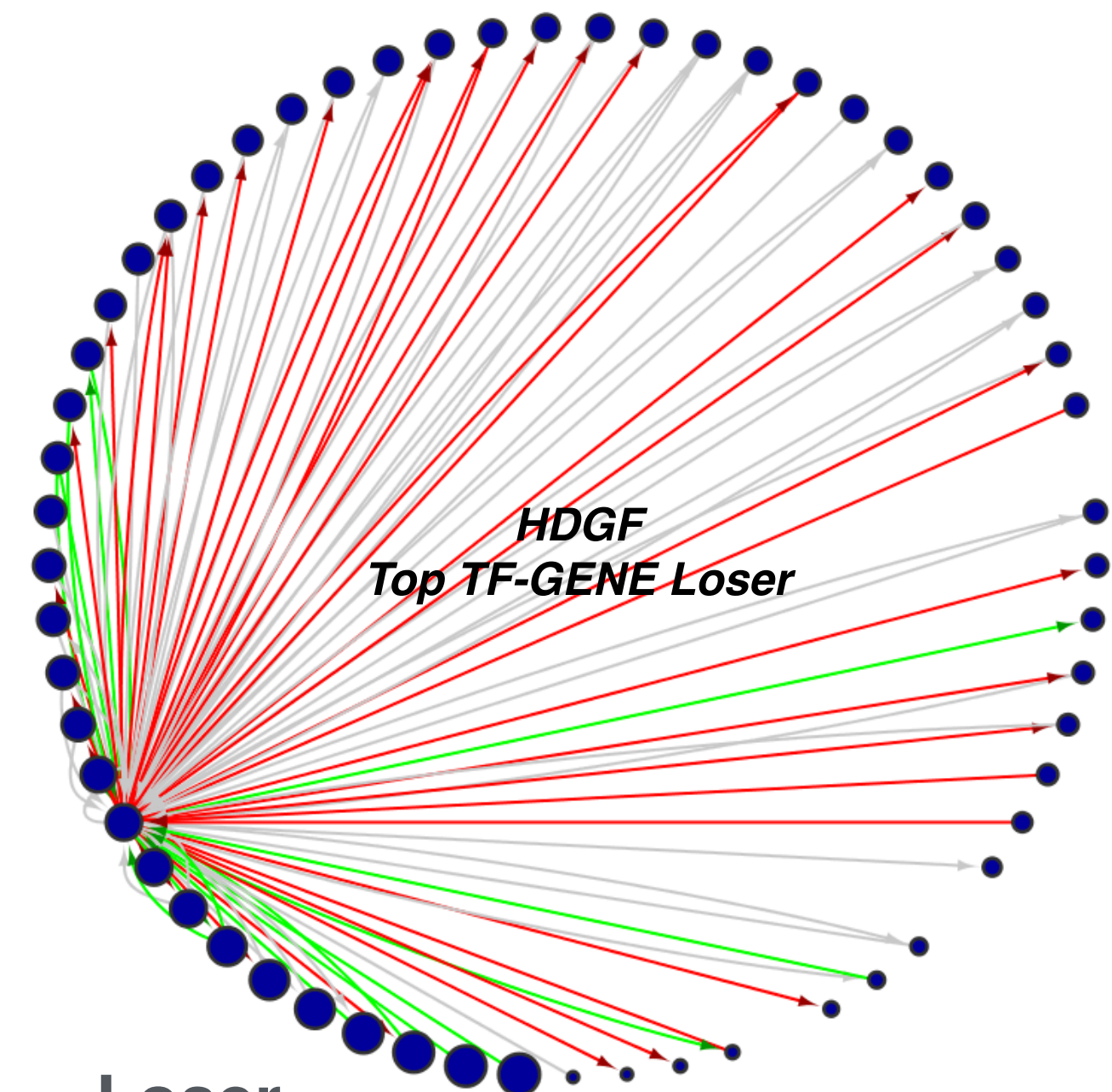
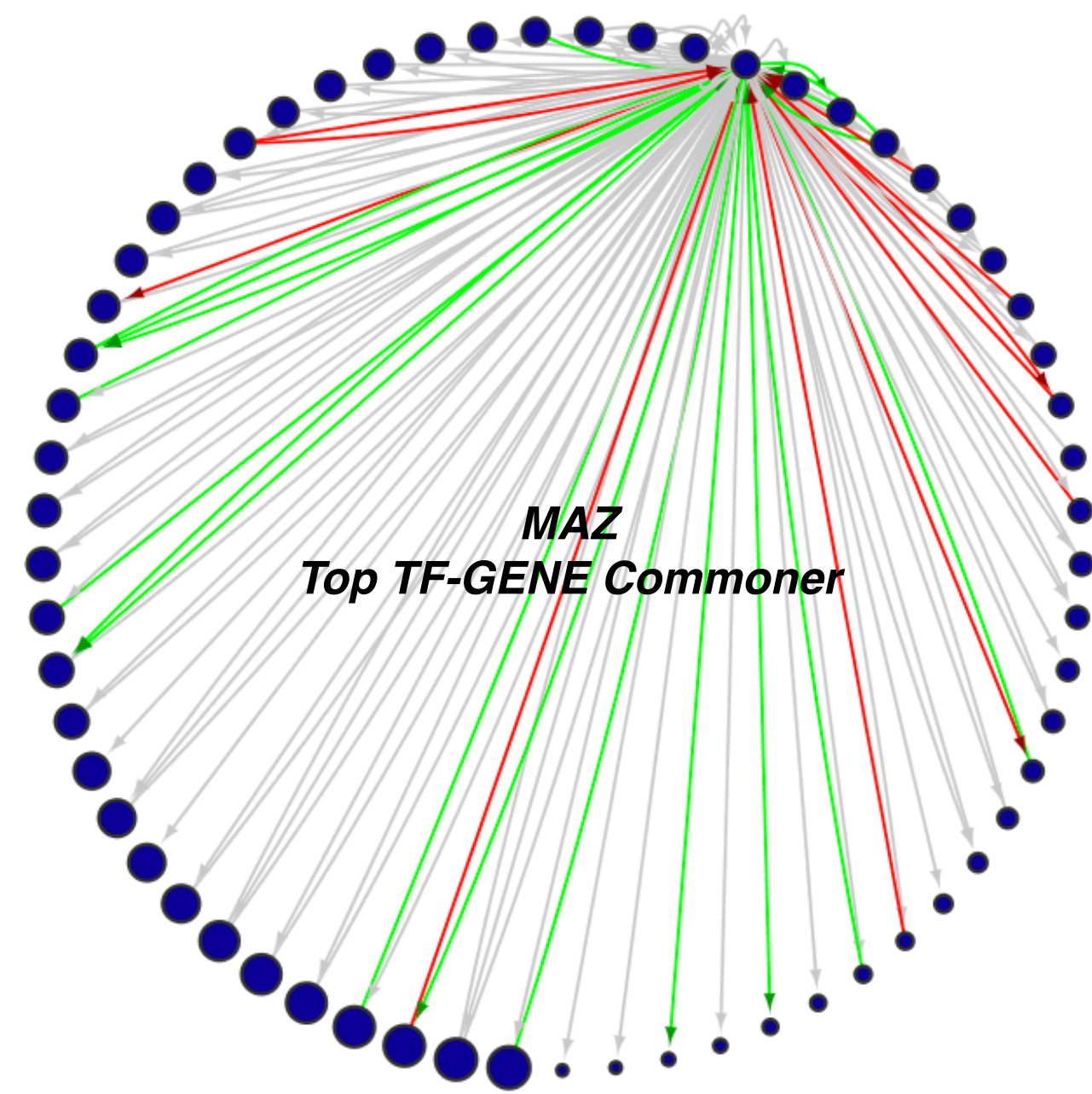
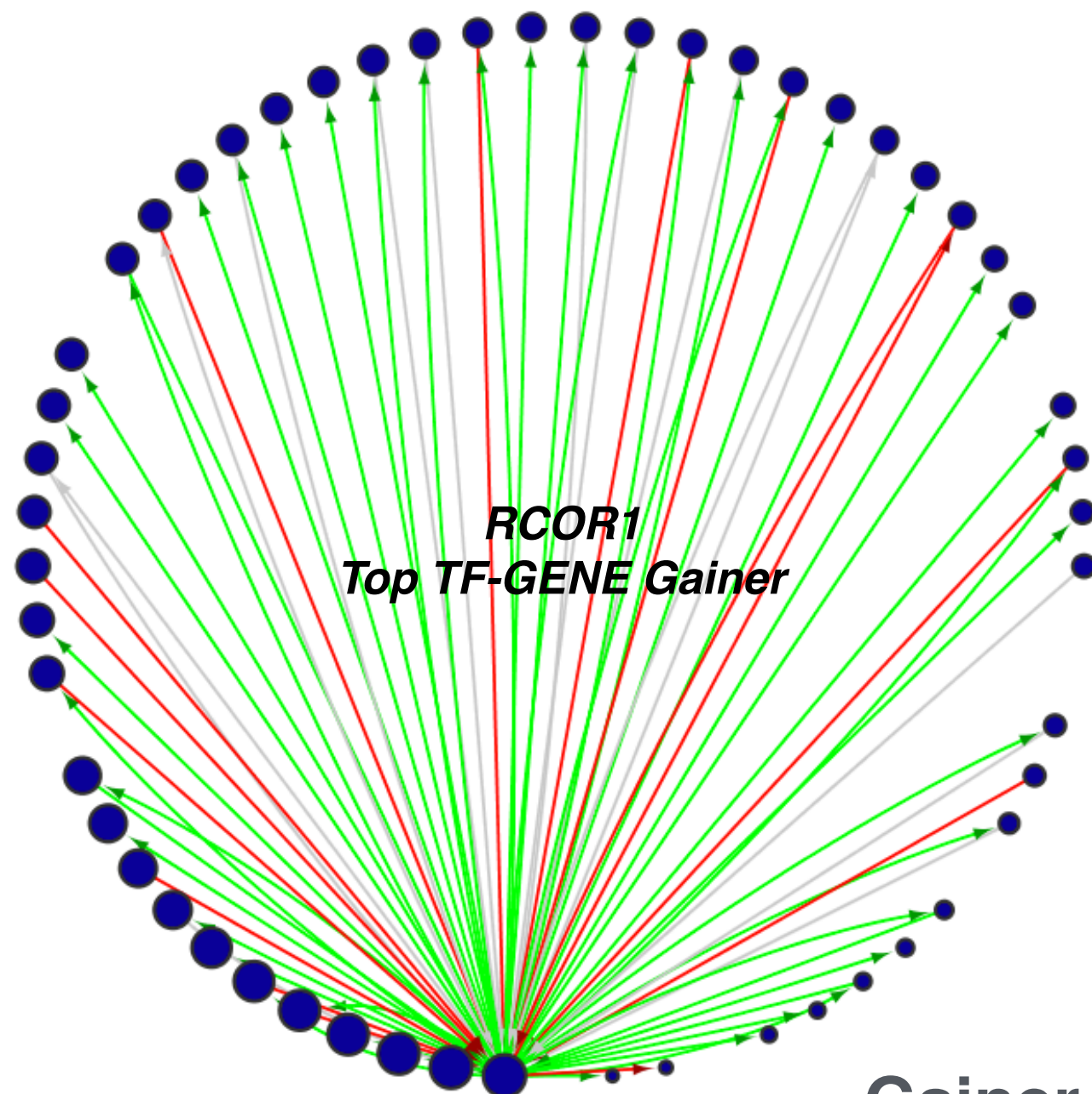


Outbound

Inbound

Gainer

Loser

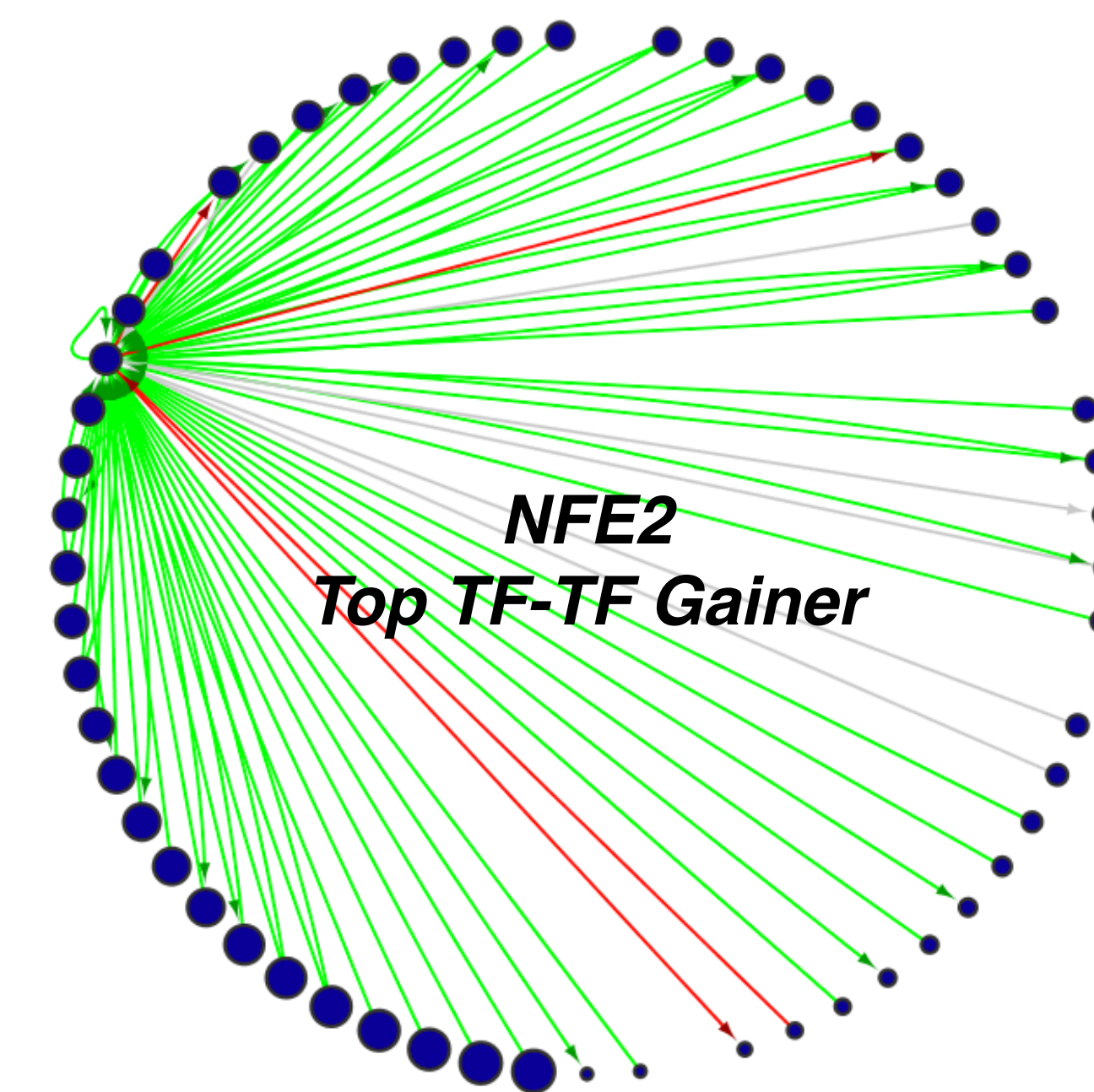
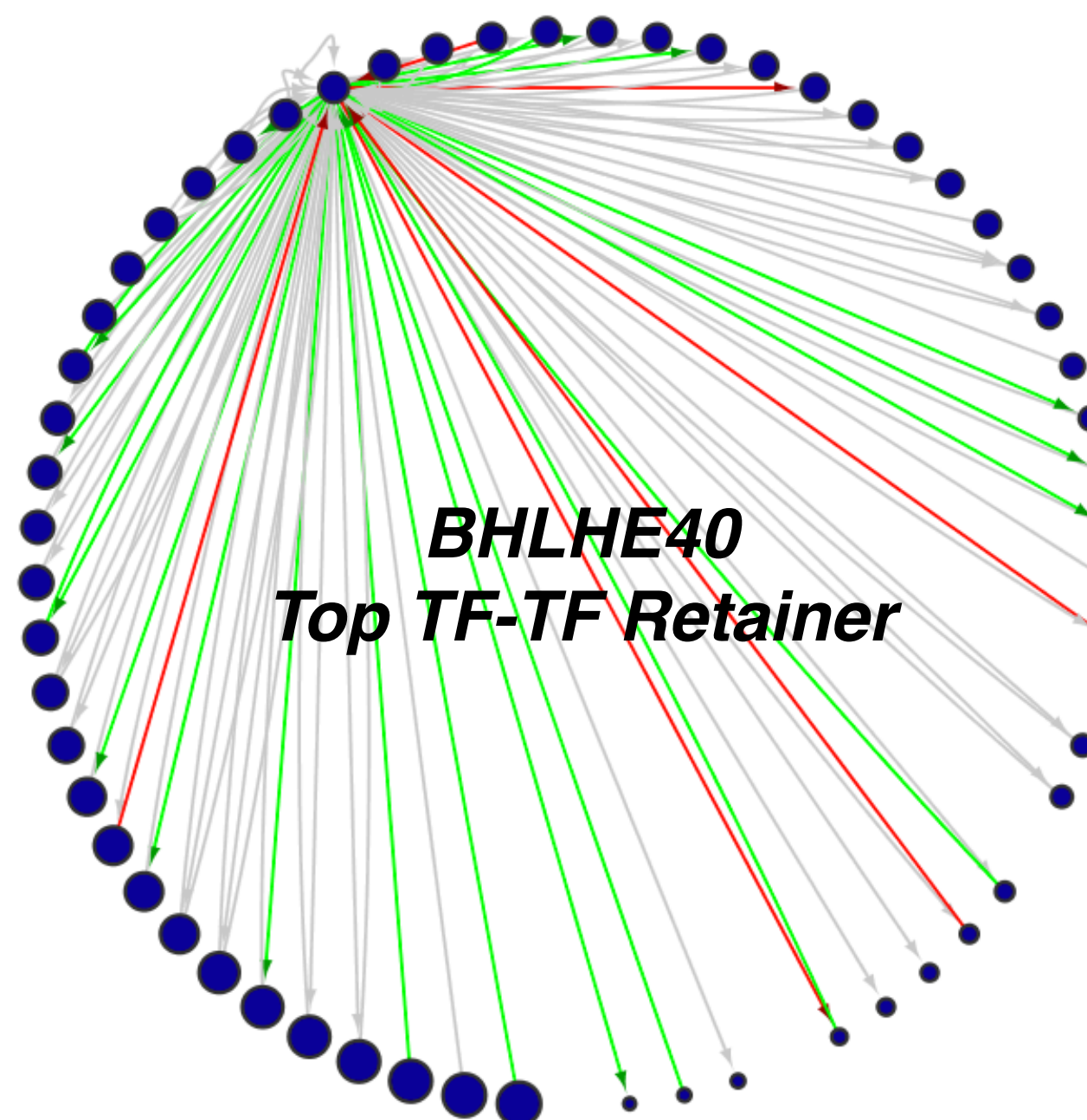
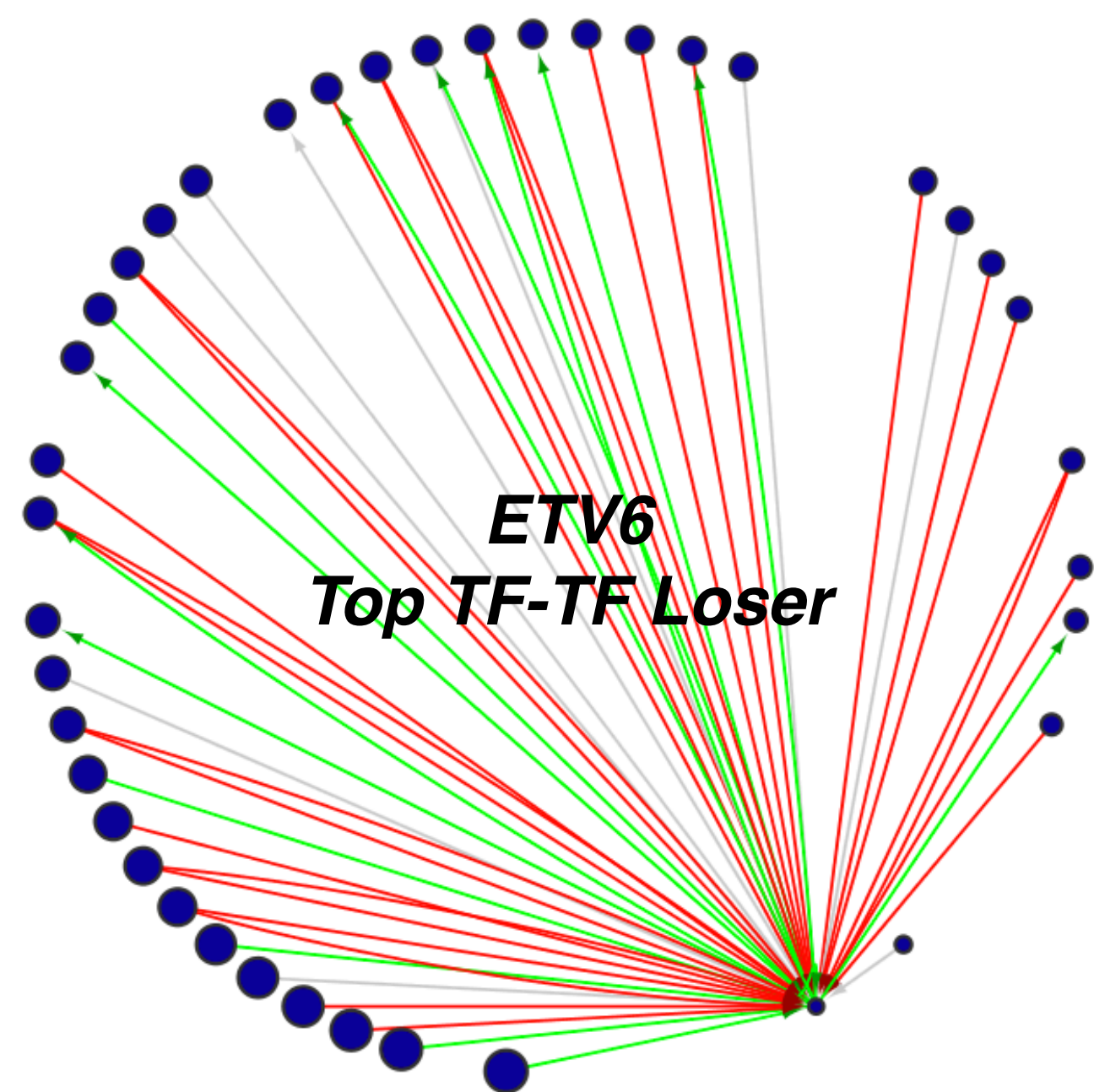
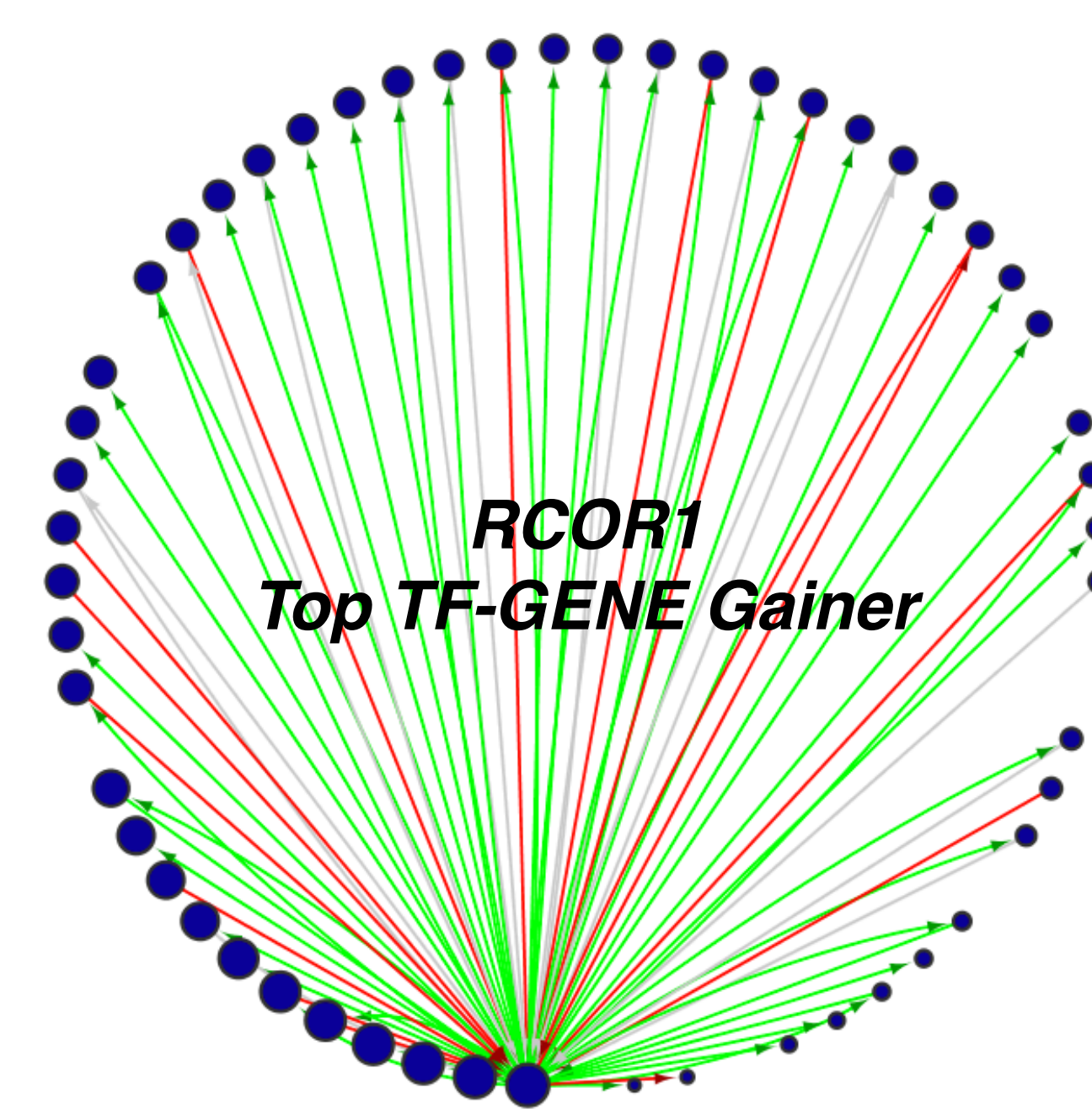
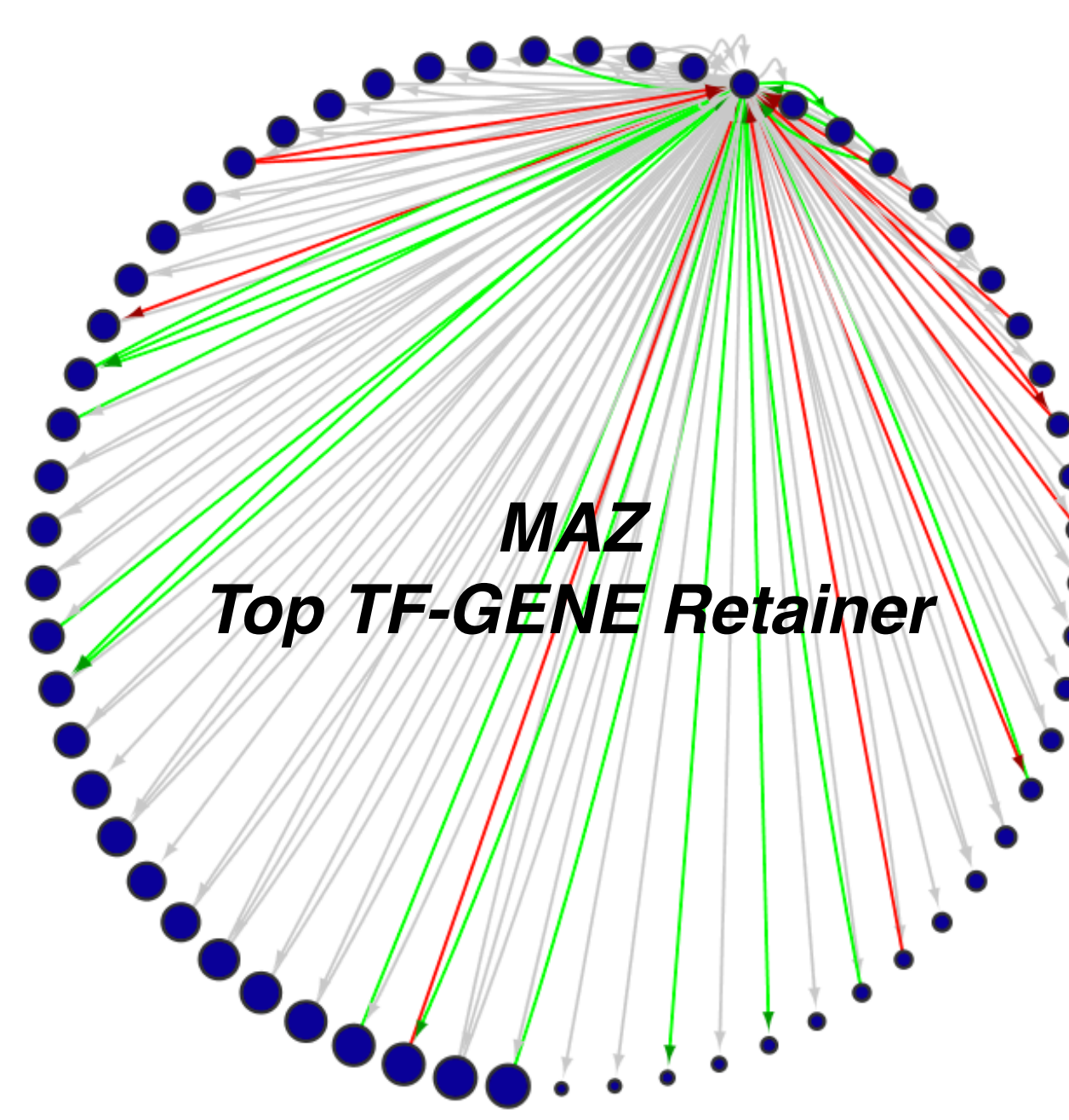
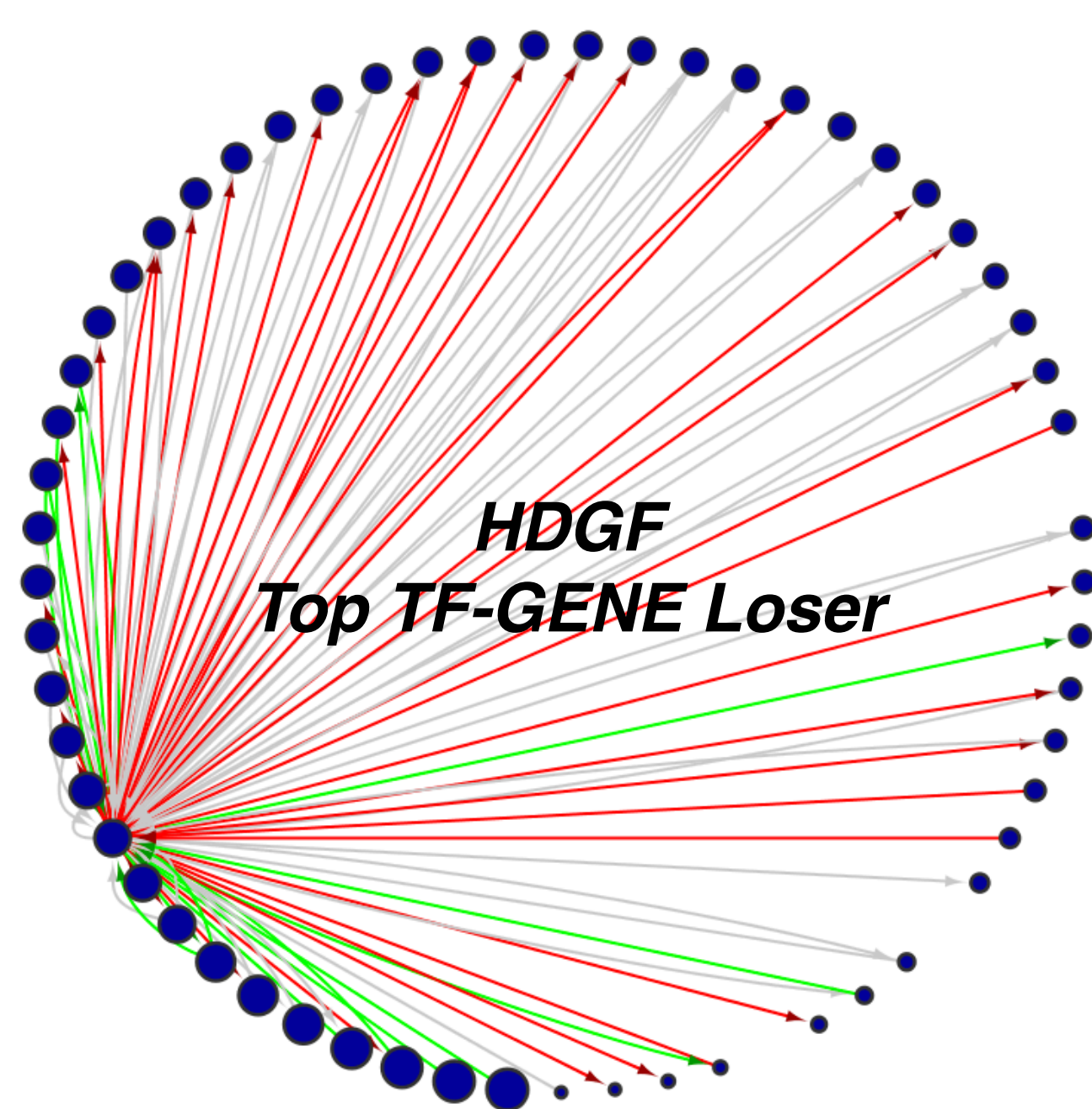


TF-GENE ↑

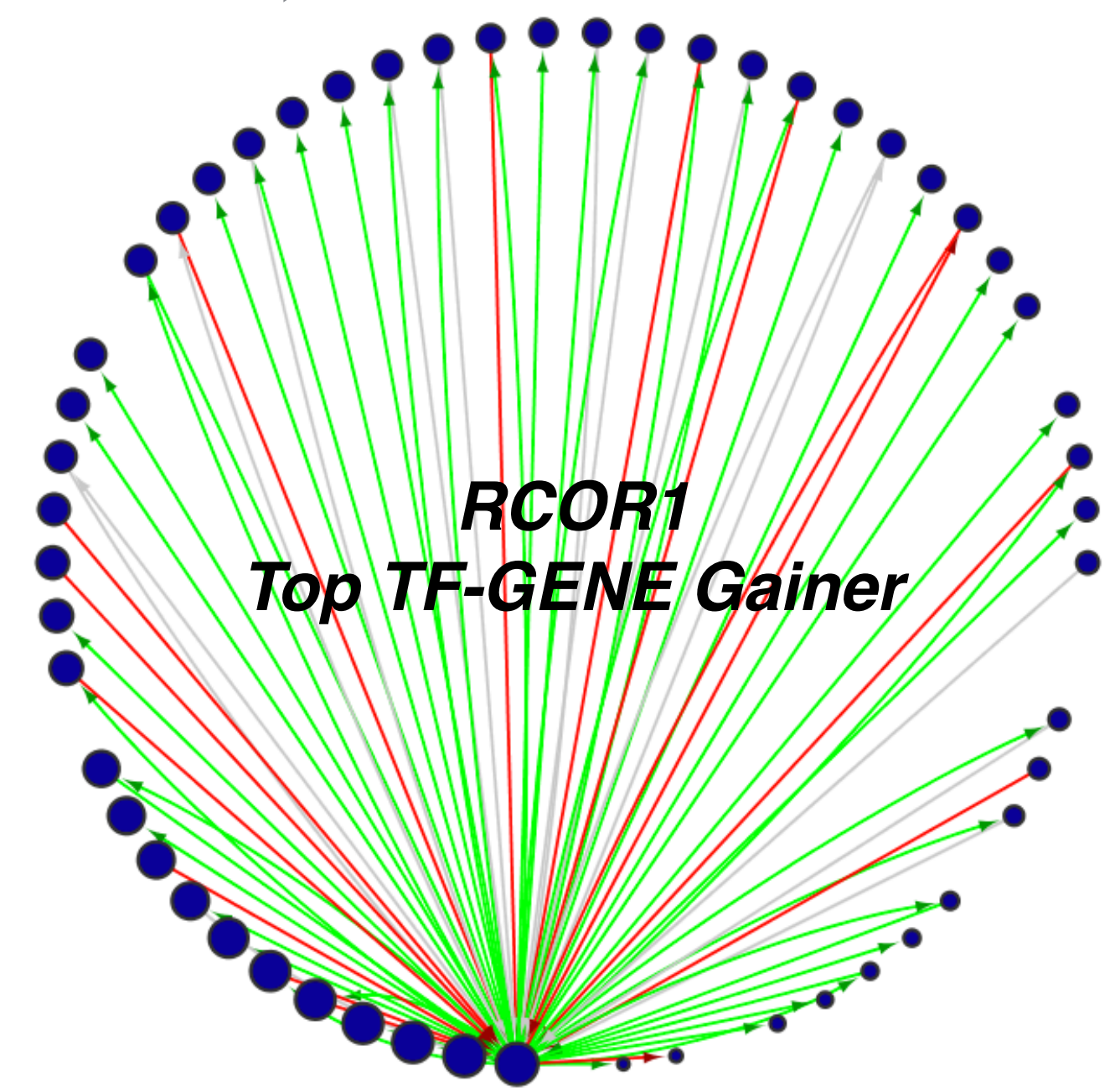
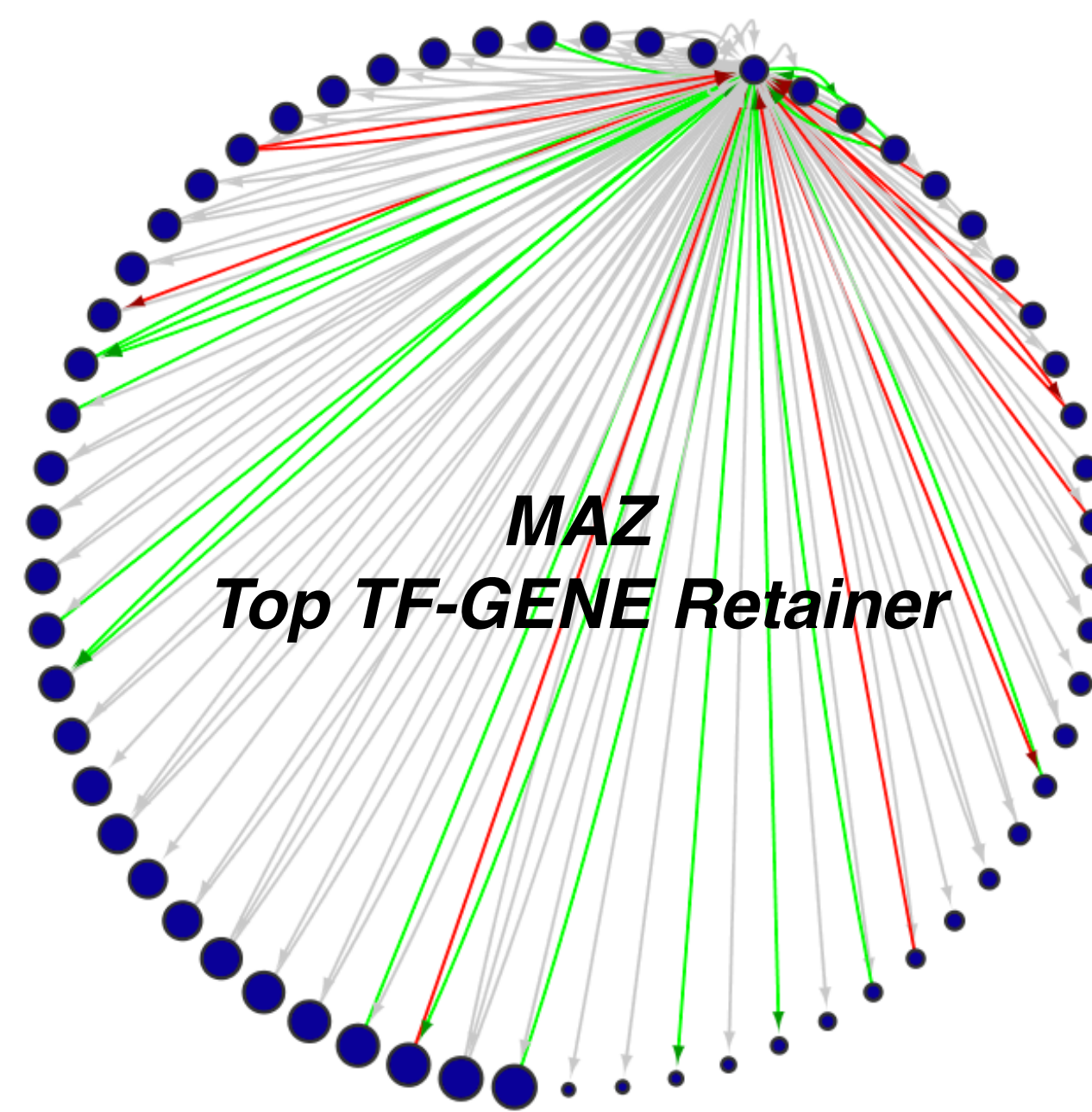
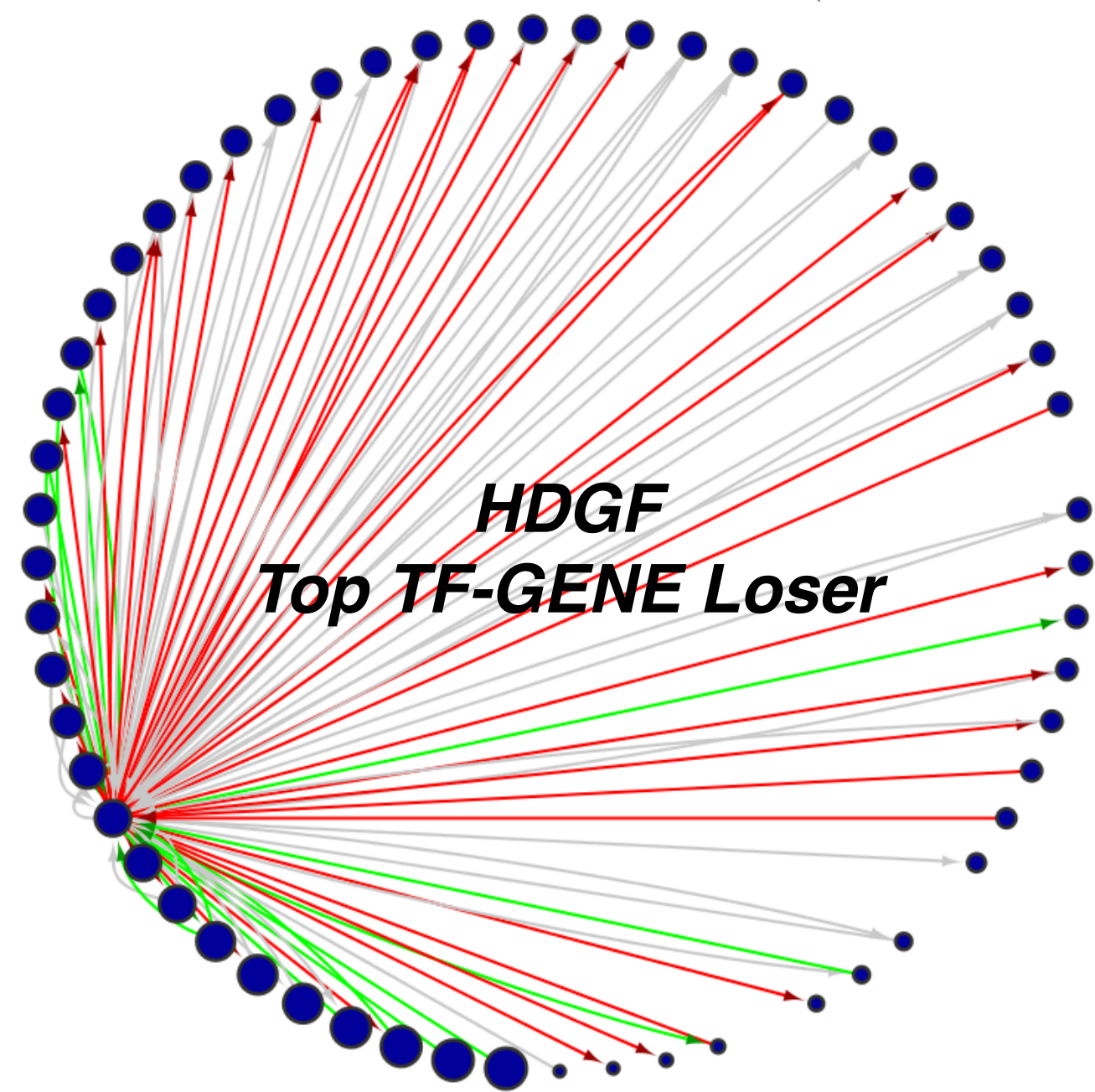
TF-TF ↓

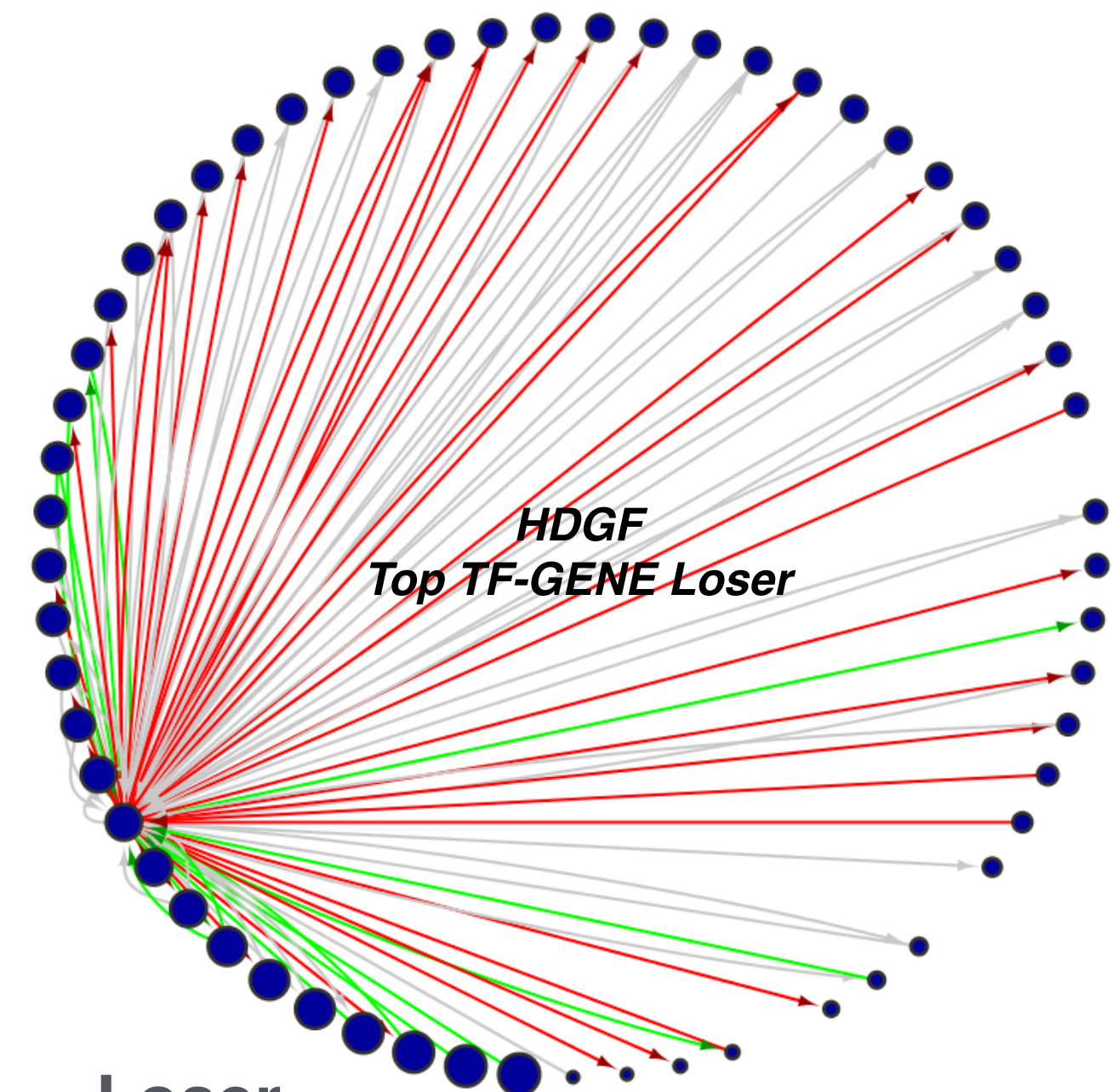
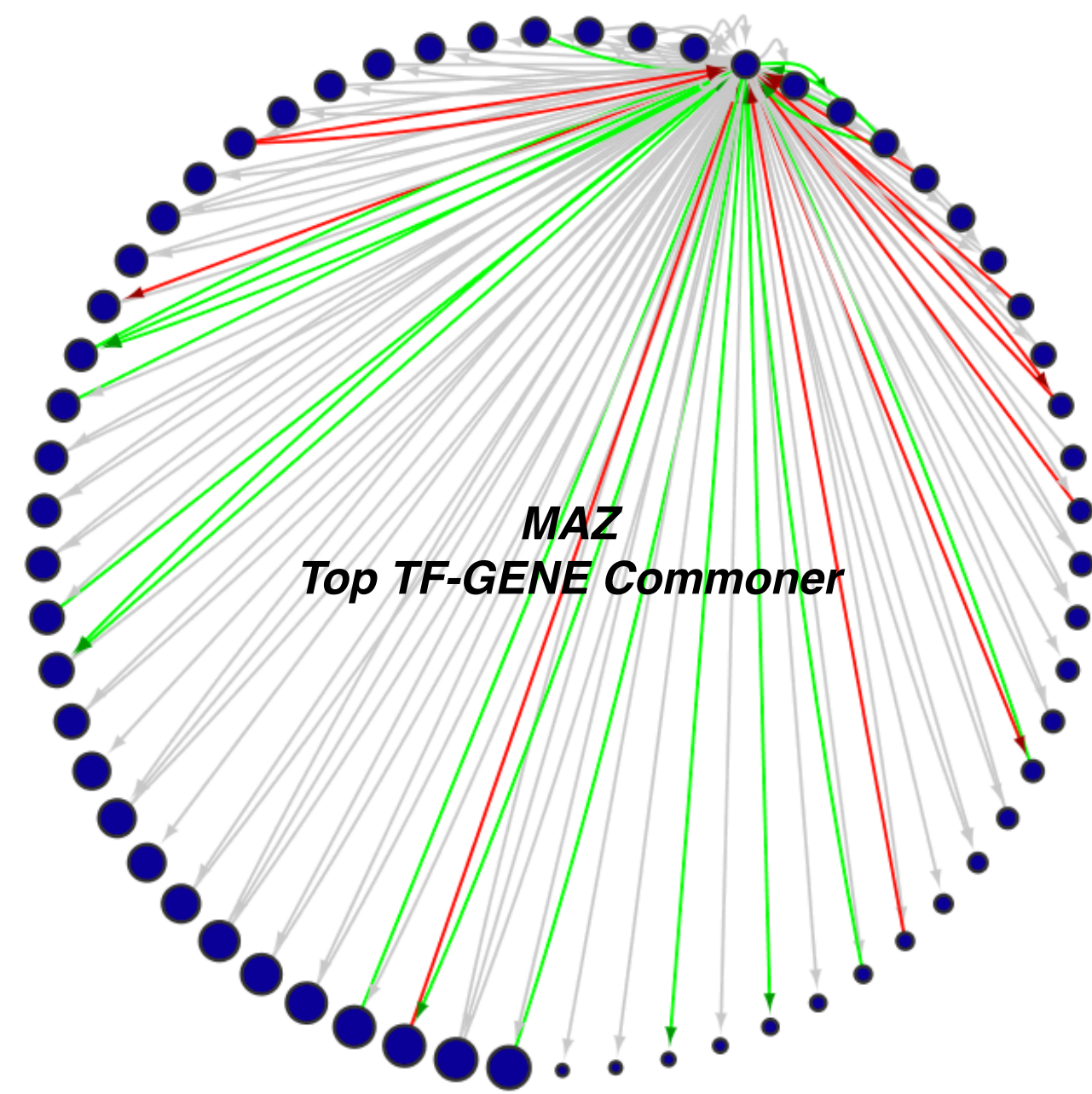
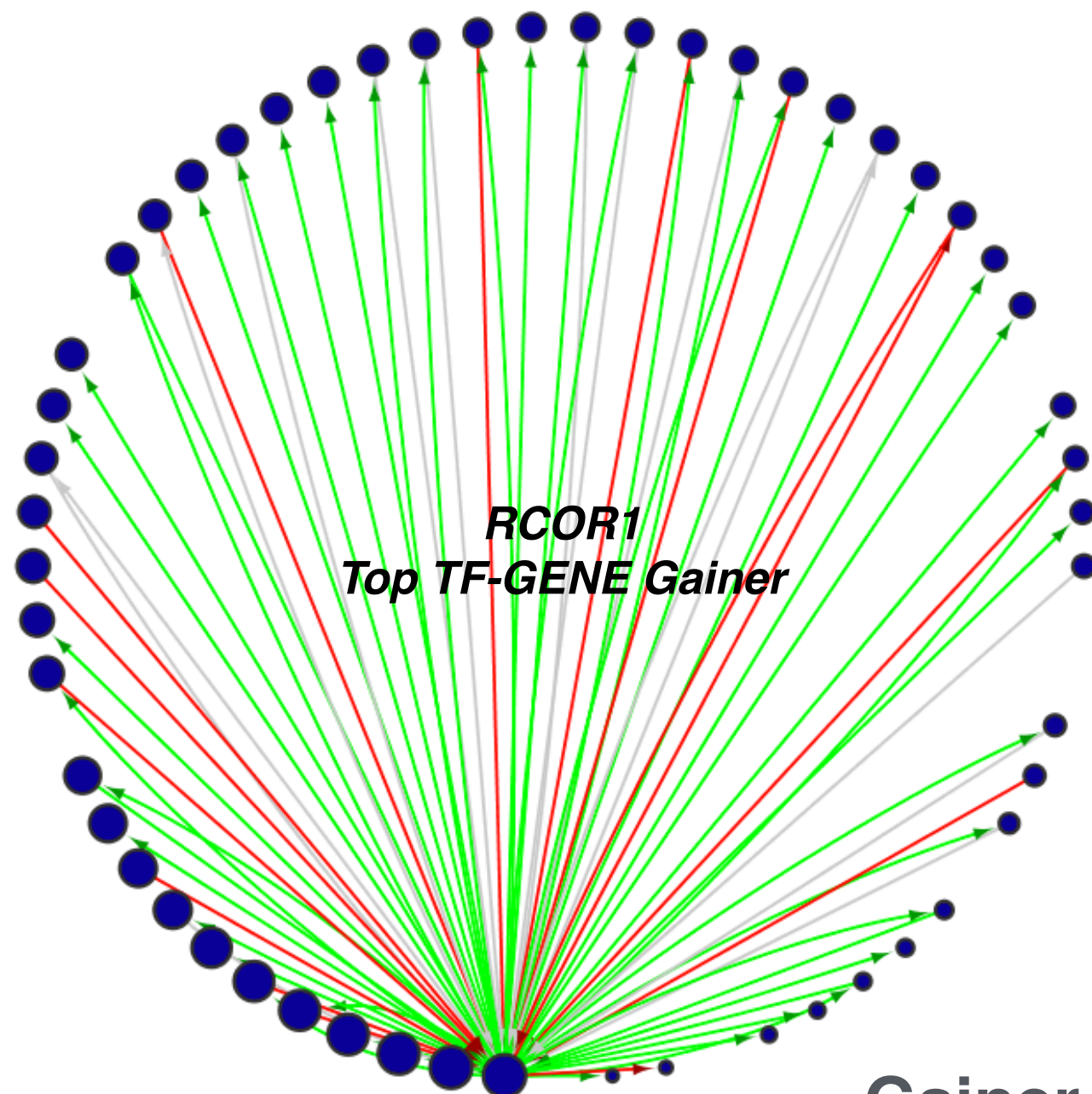
Gainer ←

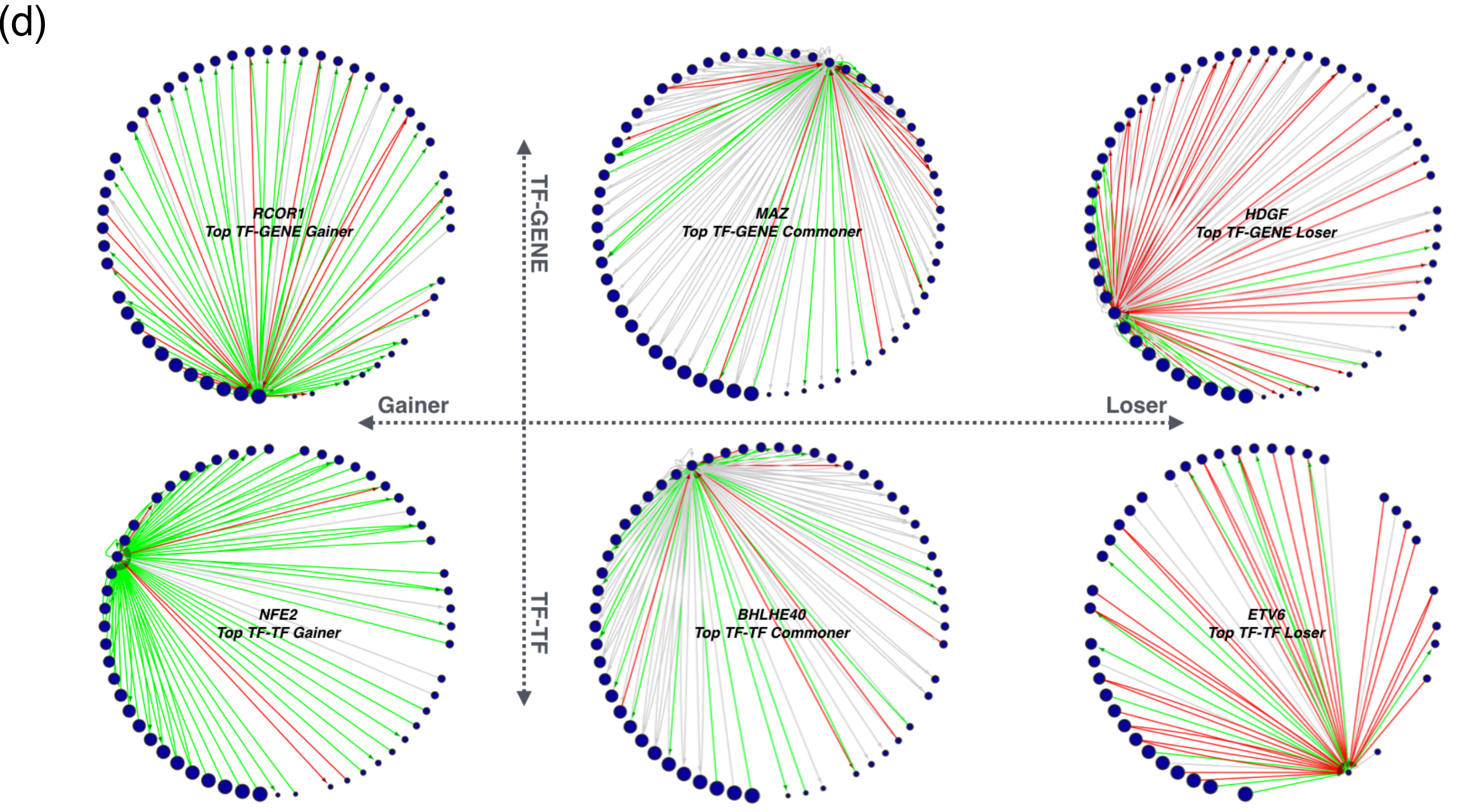
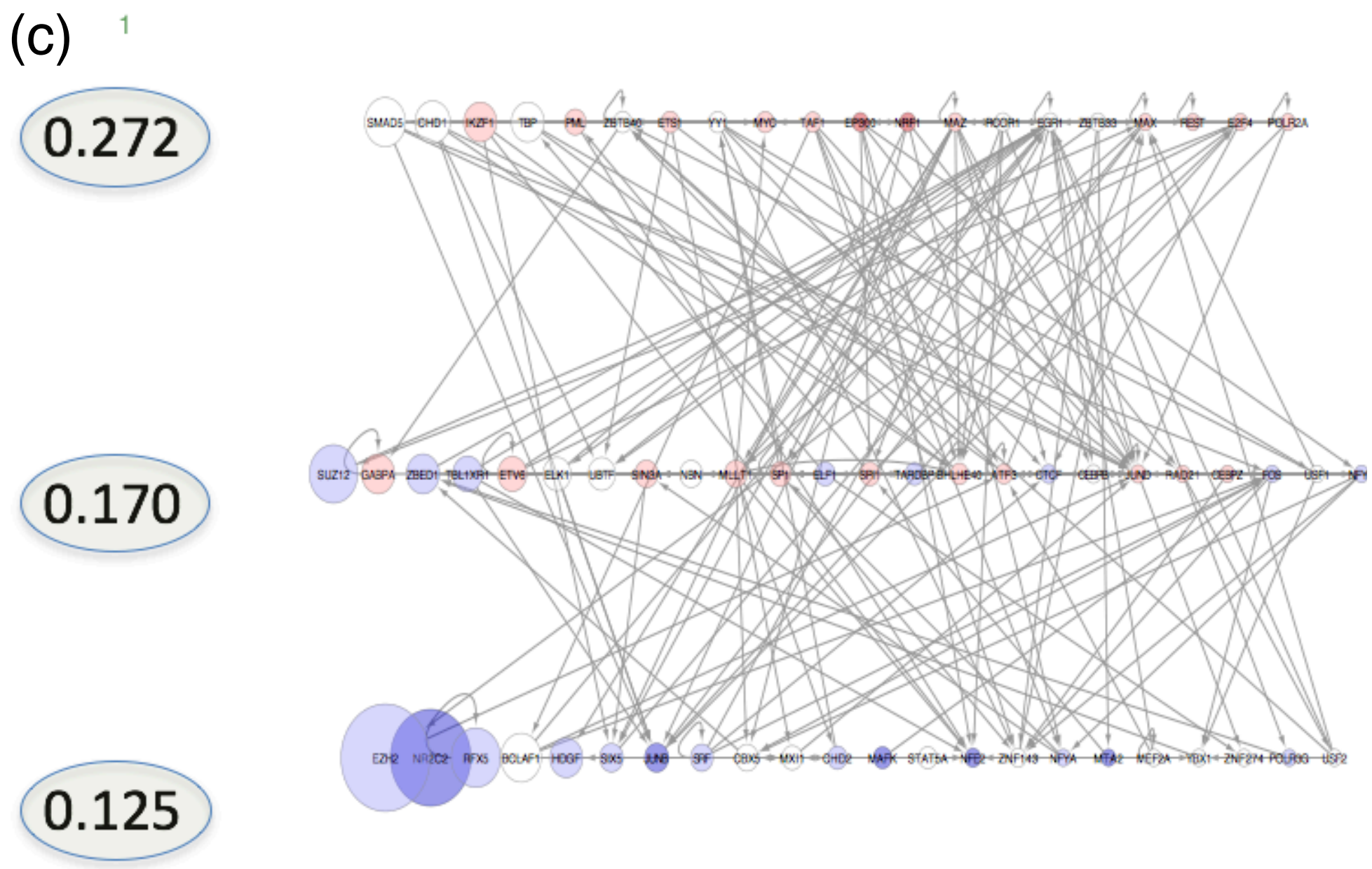
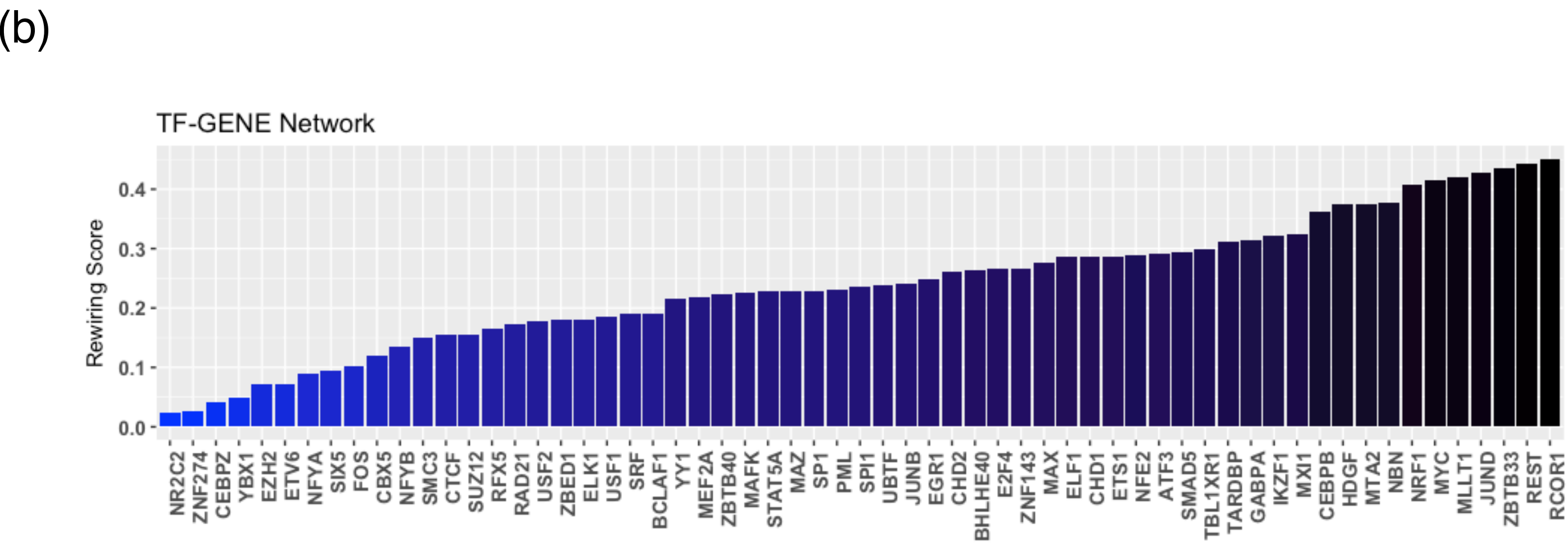
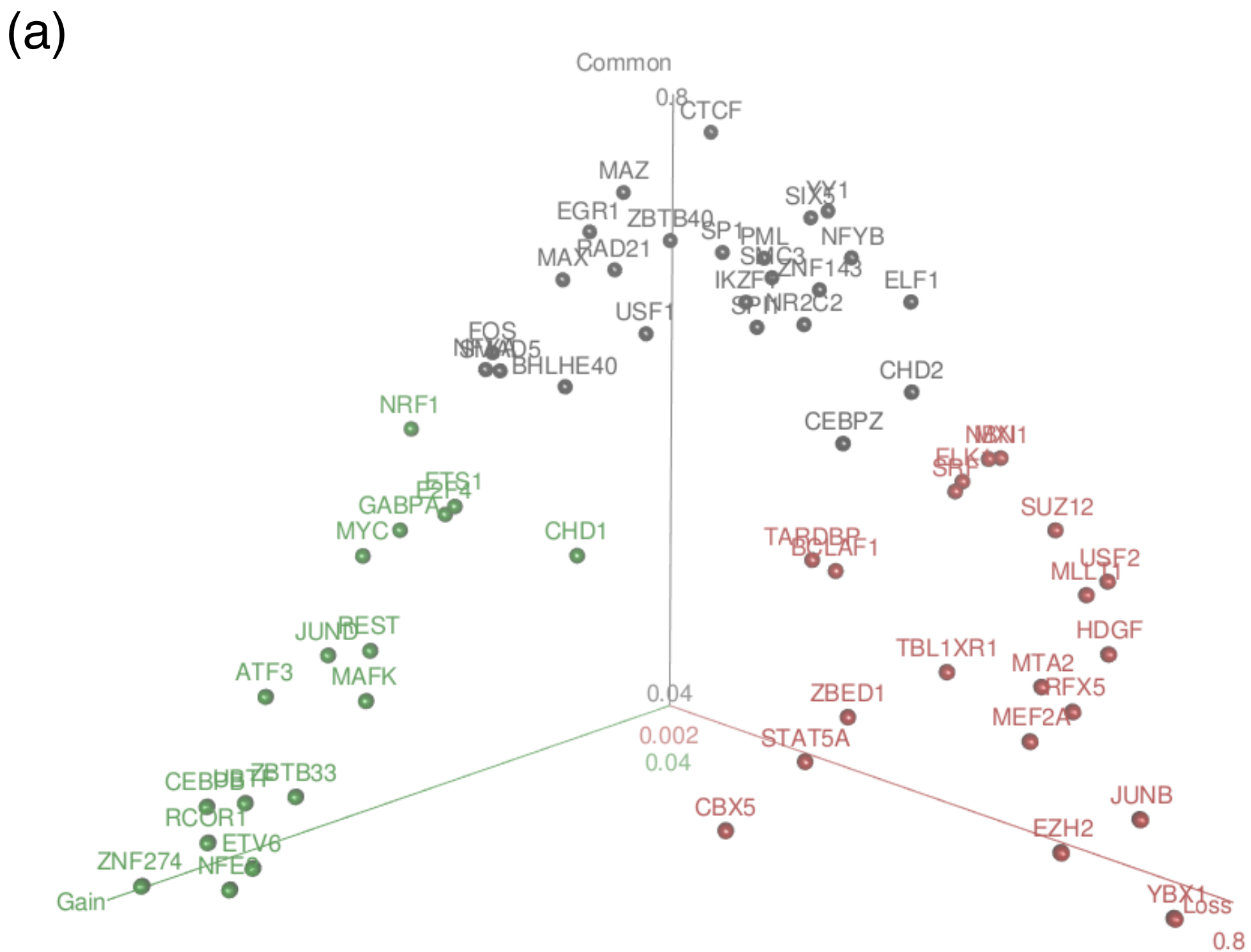
→ Loser

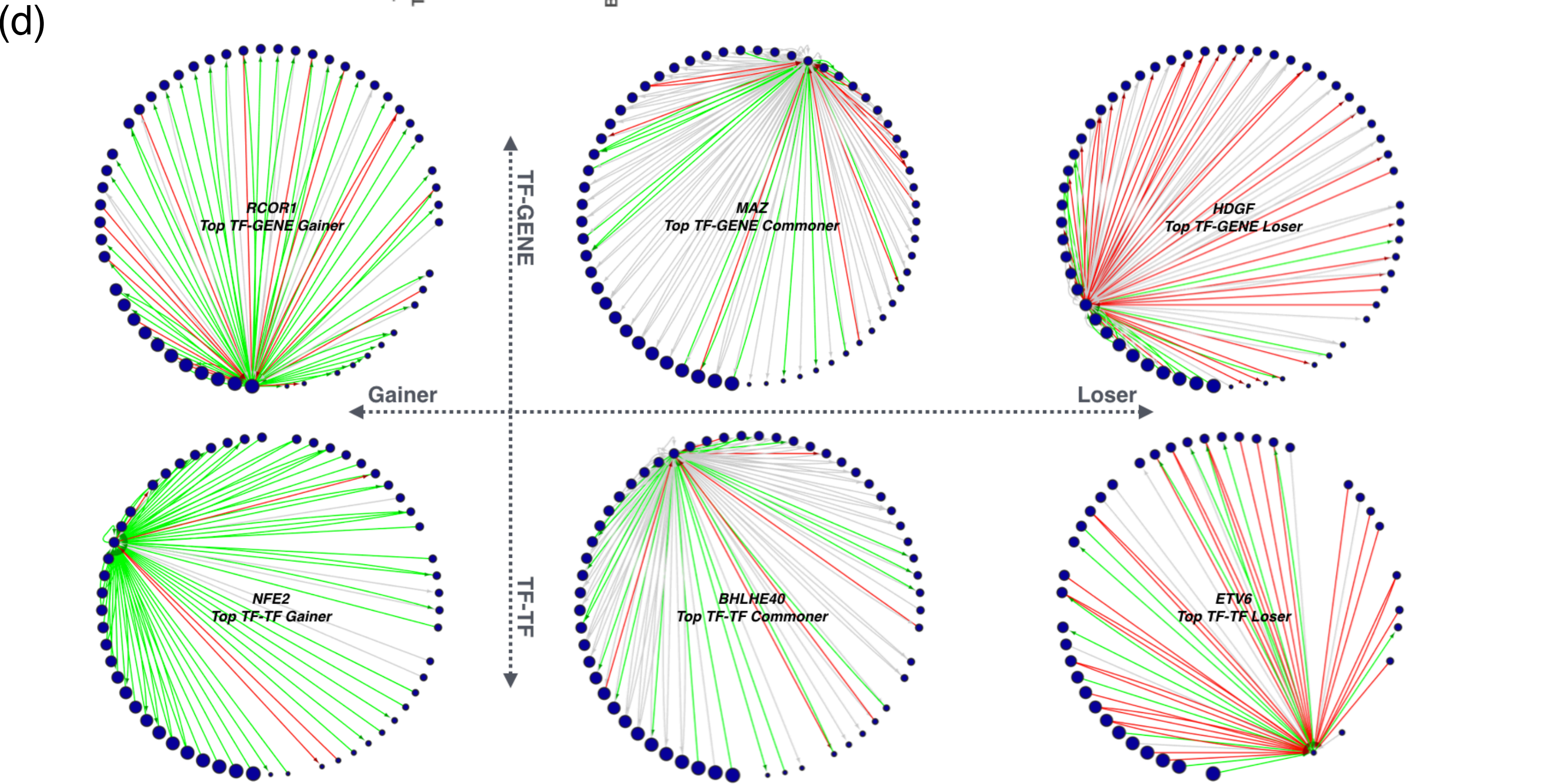
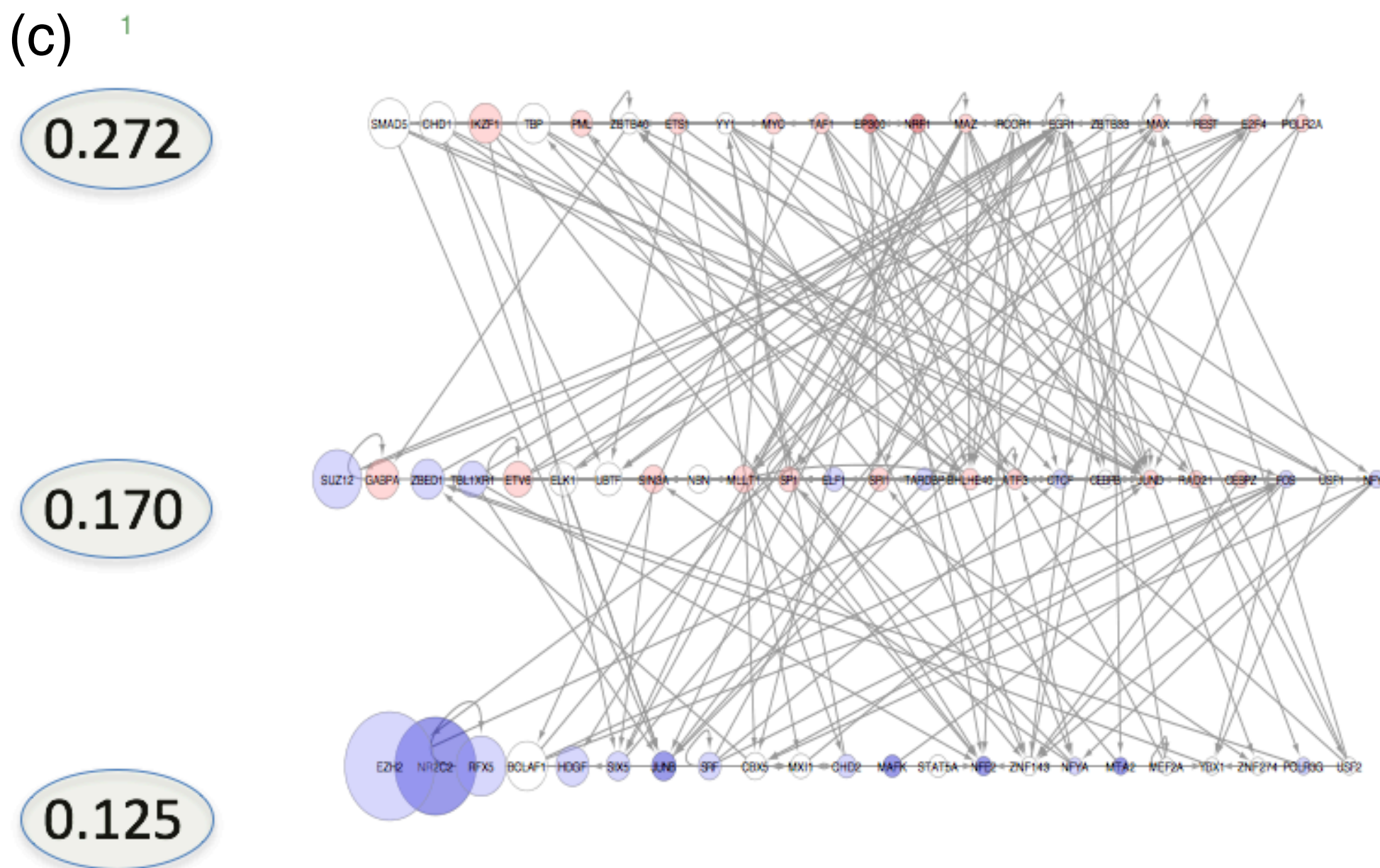
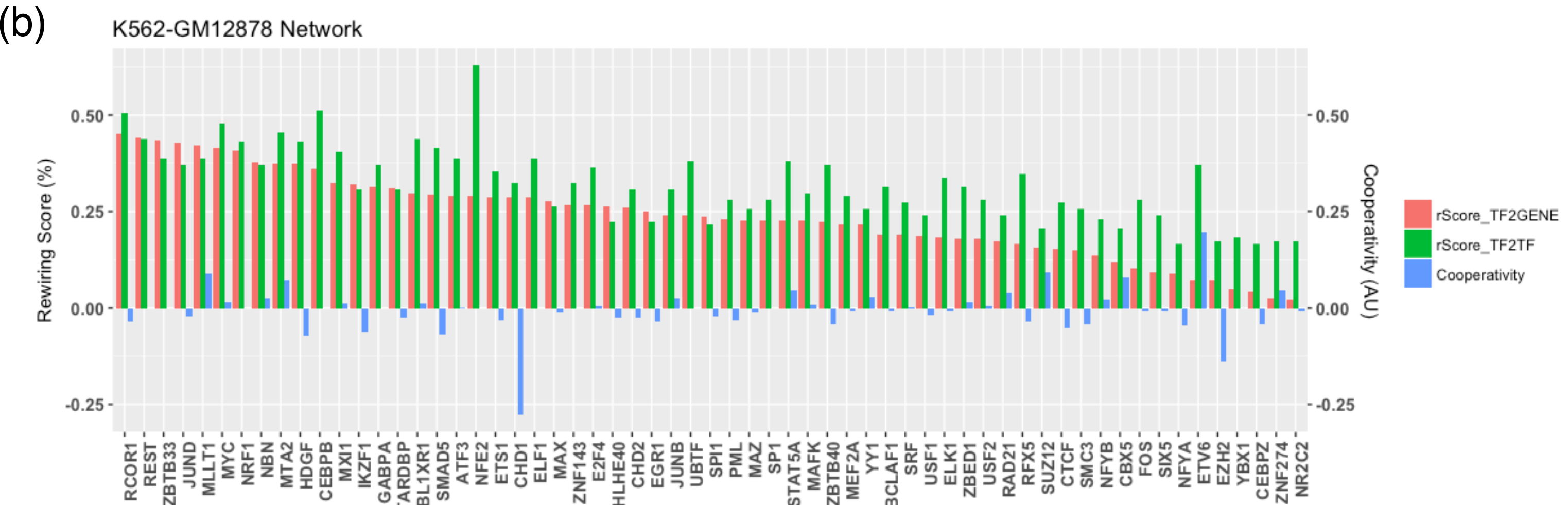
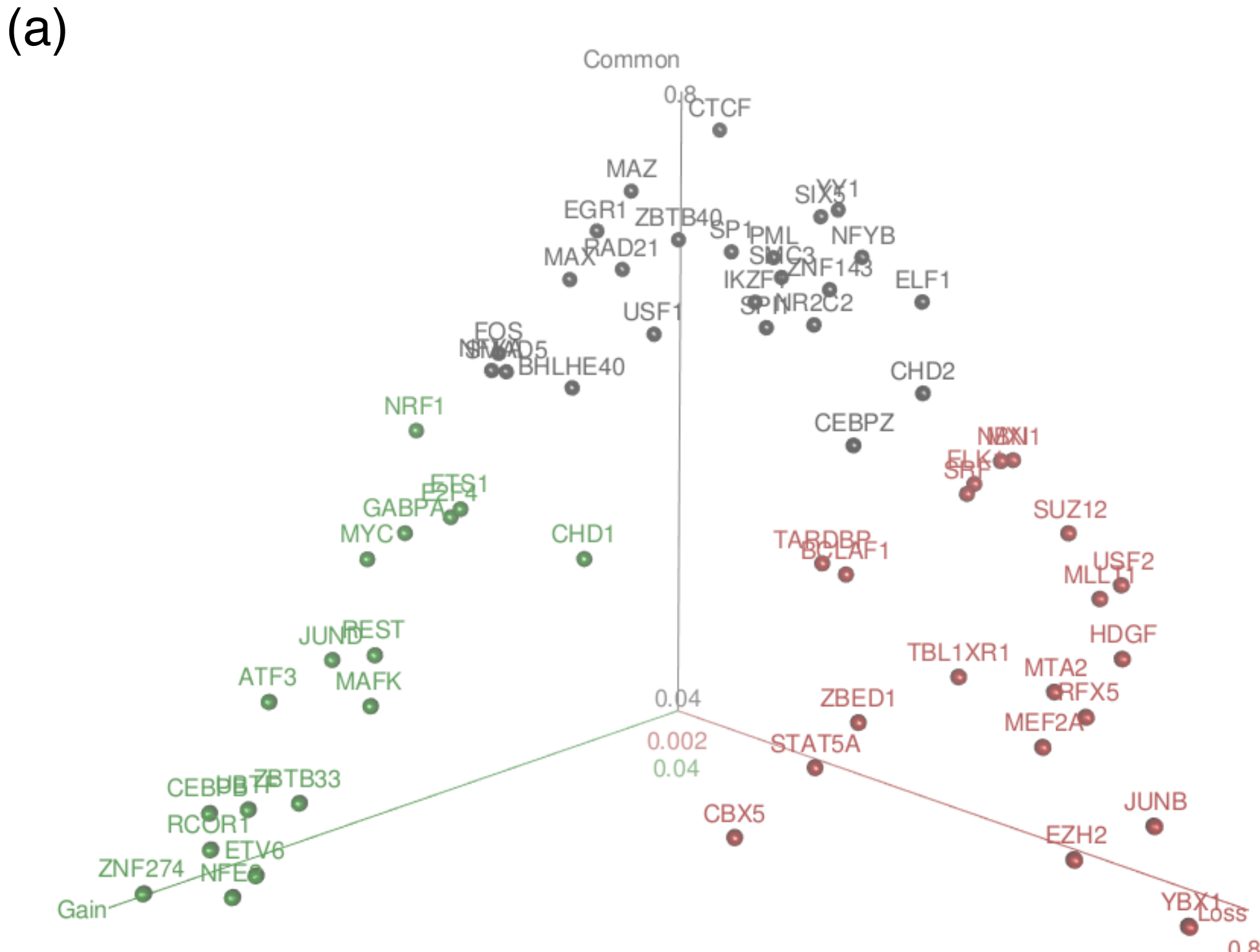


Loser ← *TF-GENE Network* → **Gainer**

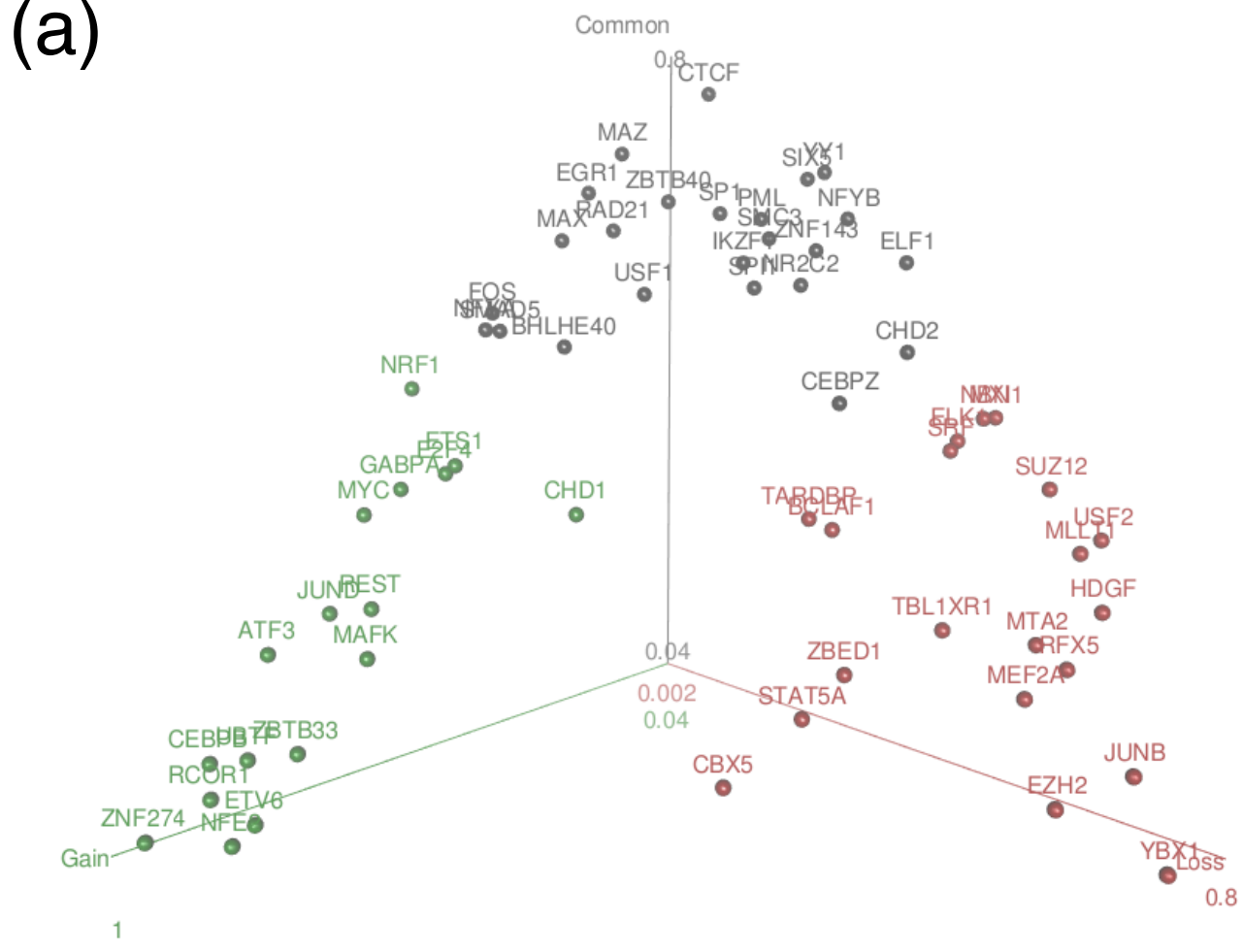




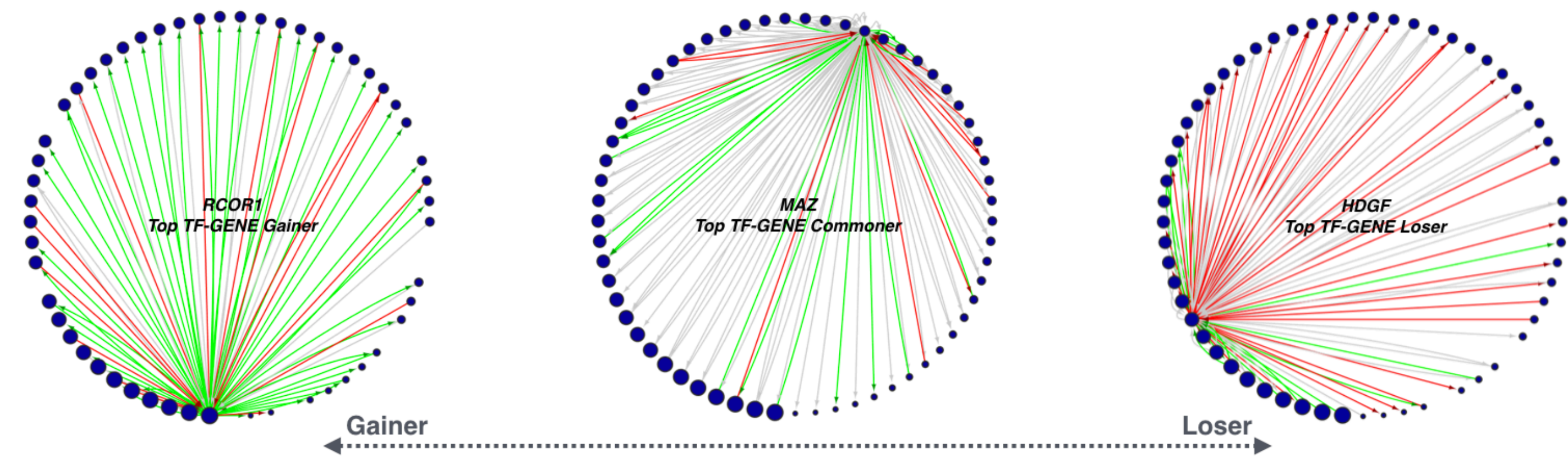




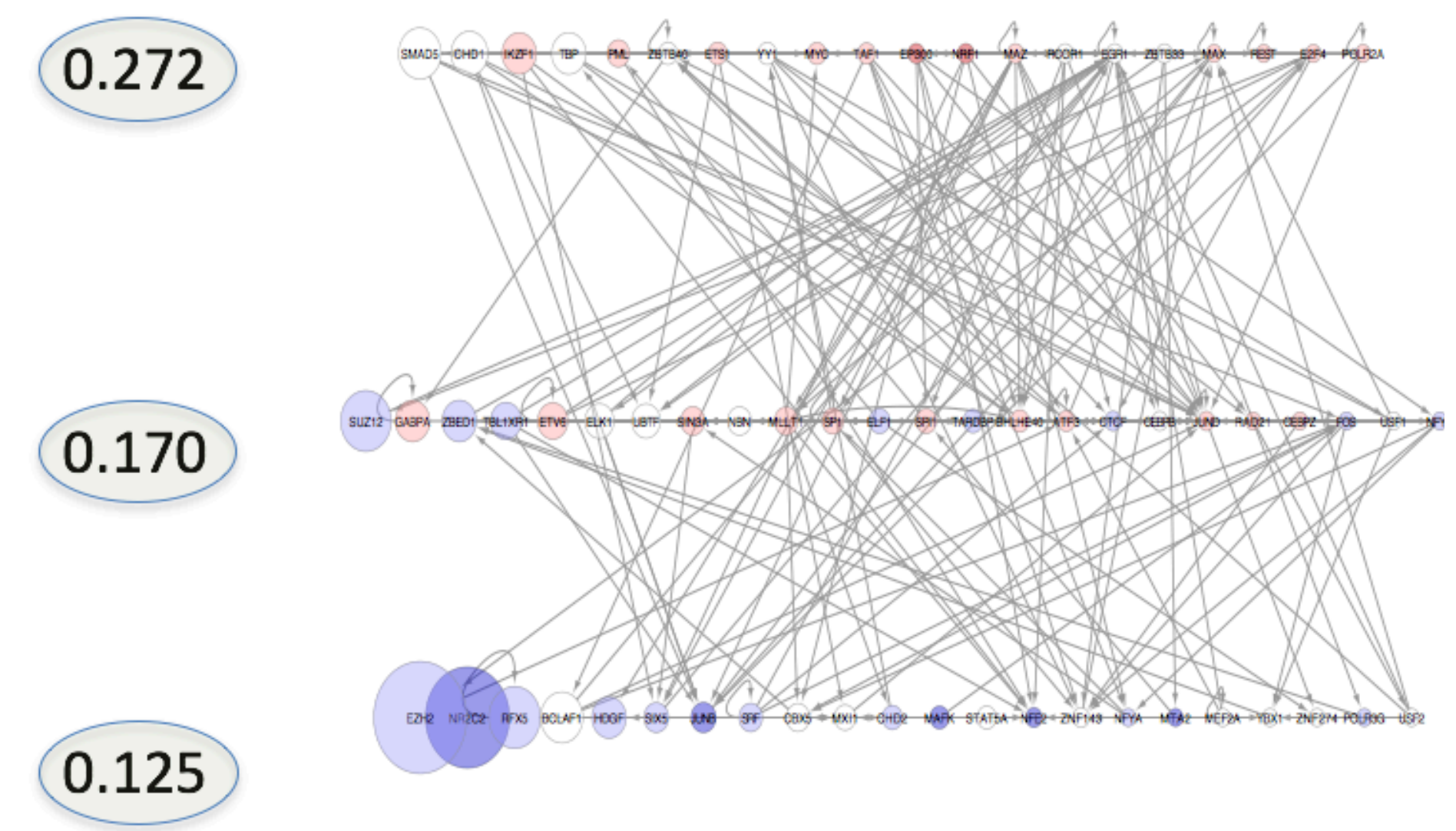
(a)



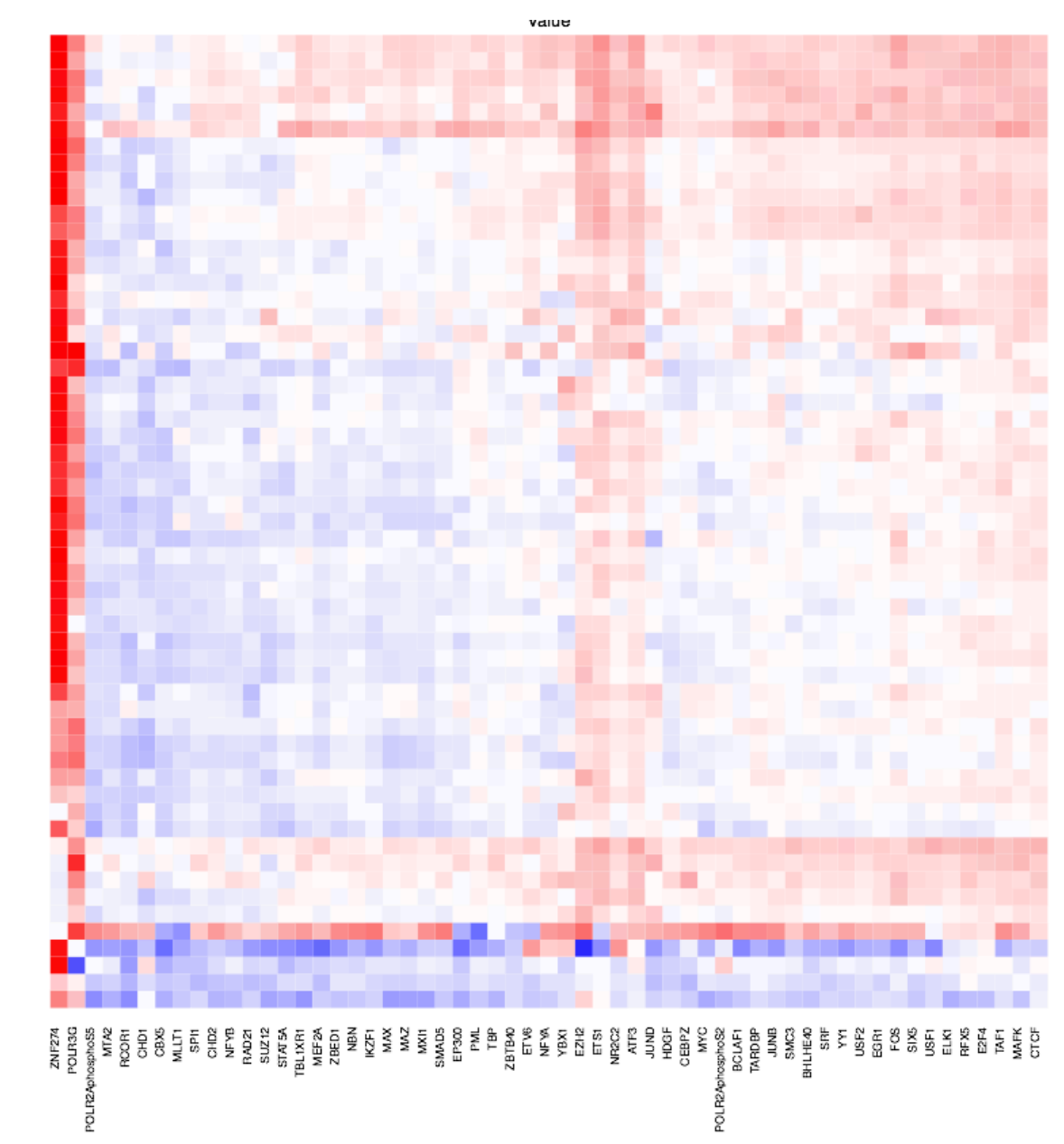
(b)



(c)



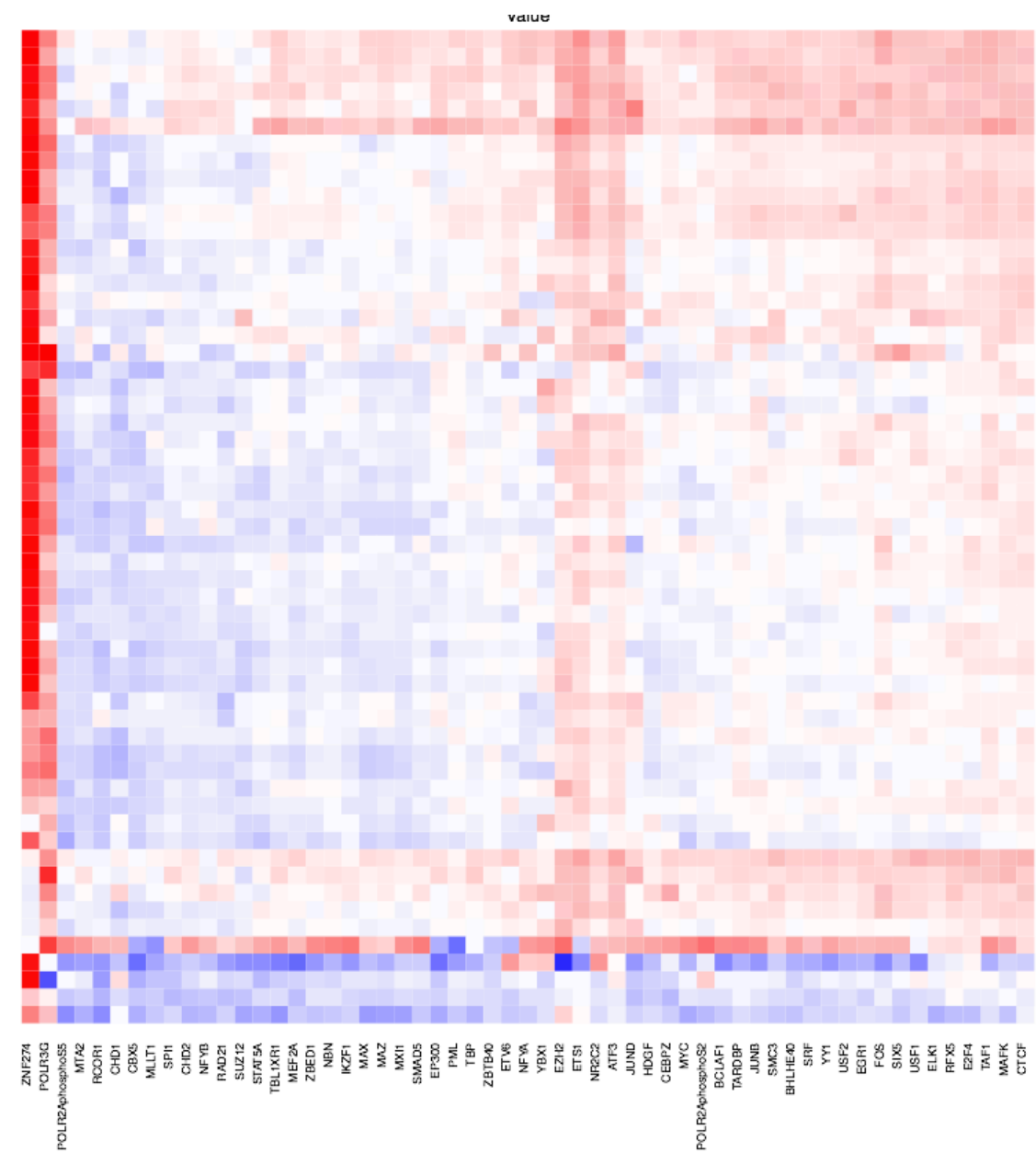
(d)



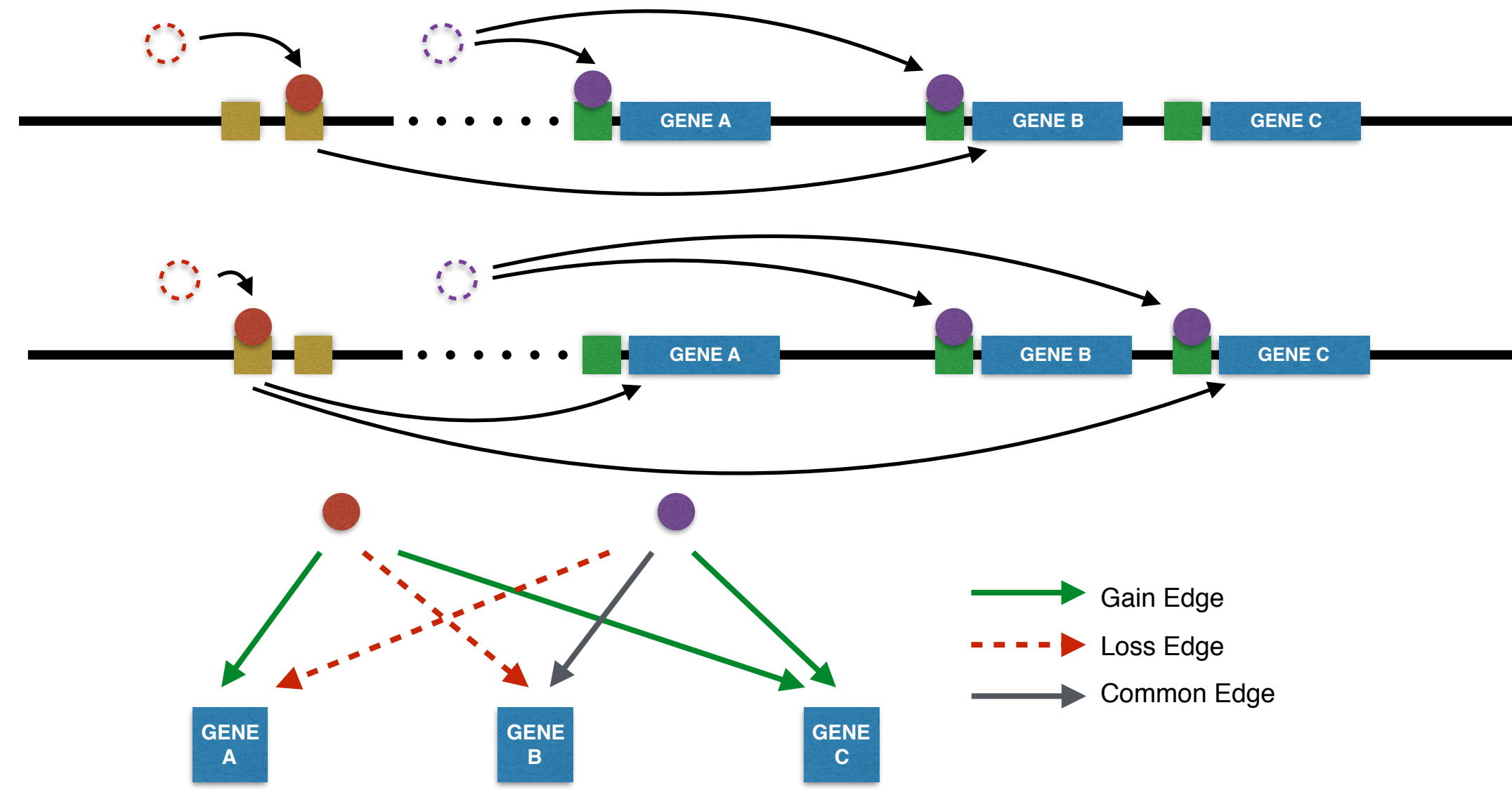
MTA2
STAT5A
MYC
RCOR1
SUZ12
POLR2AphosphoS5
SMI1
NBN
ZBED1
TBL1XR1
MAX
MAZ
IKZF1
SPI1
MEF2A
RAD21
JUNJ
FOS
YBX1
NRXG2
SIX5
ATF3
MAFK
NFYA
NFYB
POLR2AphosphoS2
SMAD3
CHD2
CEBPZ
JUNB
SRF
BHLHE40
USP2
EGRI1
YY1
TARDBP
BCLAF1
TAF1
SMC3
CTCF
E2F4
ELK1
RFX5
PML
TBP
ZBTB40
HDGF
CBX5
ETV6
MLL1
EP300
USP1
ZNF274
POLR3G
EZH2
ETS1
CHD1

ZNF274
POLR3G
POLR2AphosphoS5
MAZ
MYC
SMI1
OD1
CBX5
MLL1
SPI1
NFYB
RAD21
SUZ12
TBL1XR1
TBL1XR1
ZBED1
NBN
MAX
MAZ
MOT1
SMAD3
EZH2
PML
TBP
ZBTB40
HDGF
MYC
YBX1
E2F4
ETS1
JUNJ
HDGF
CEBPZ
POLR2AphosphoS2
BCLAF1
TARDBP
JUNB
NBN
BHLHE40
ERF
YY1
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EDR1
FOS
SIX5
USP1
NFYB
RFX5
E2F4
TAF1
MAFK
CTCF

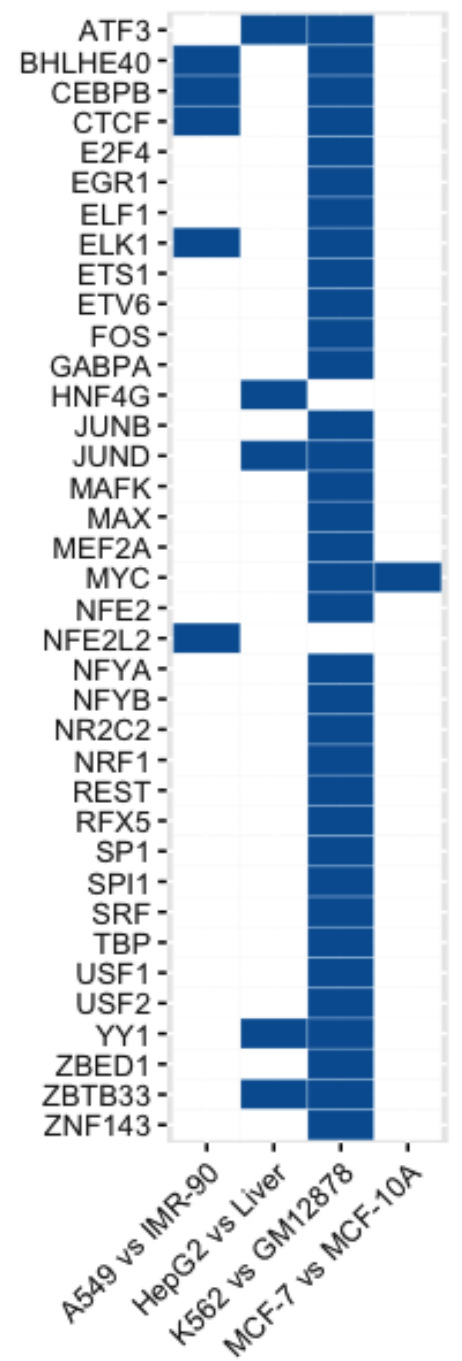
(a)



(b)



(c)

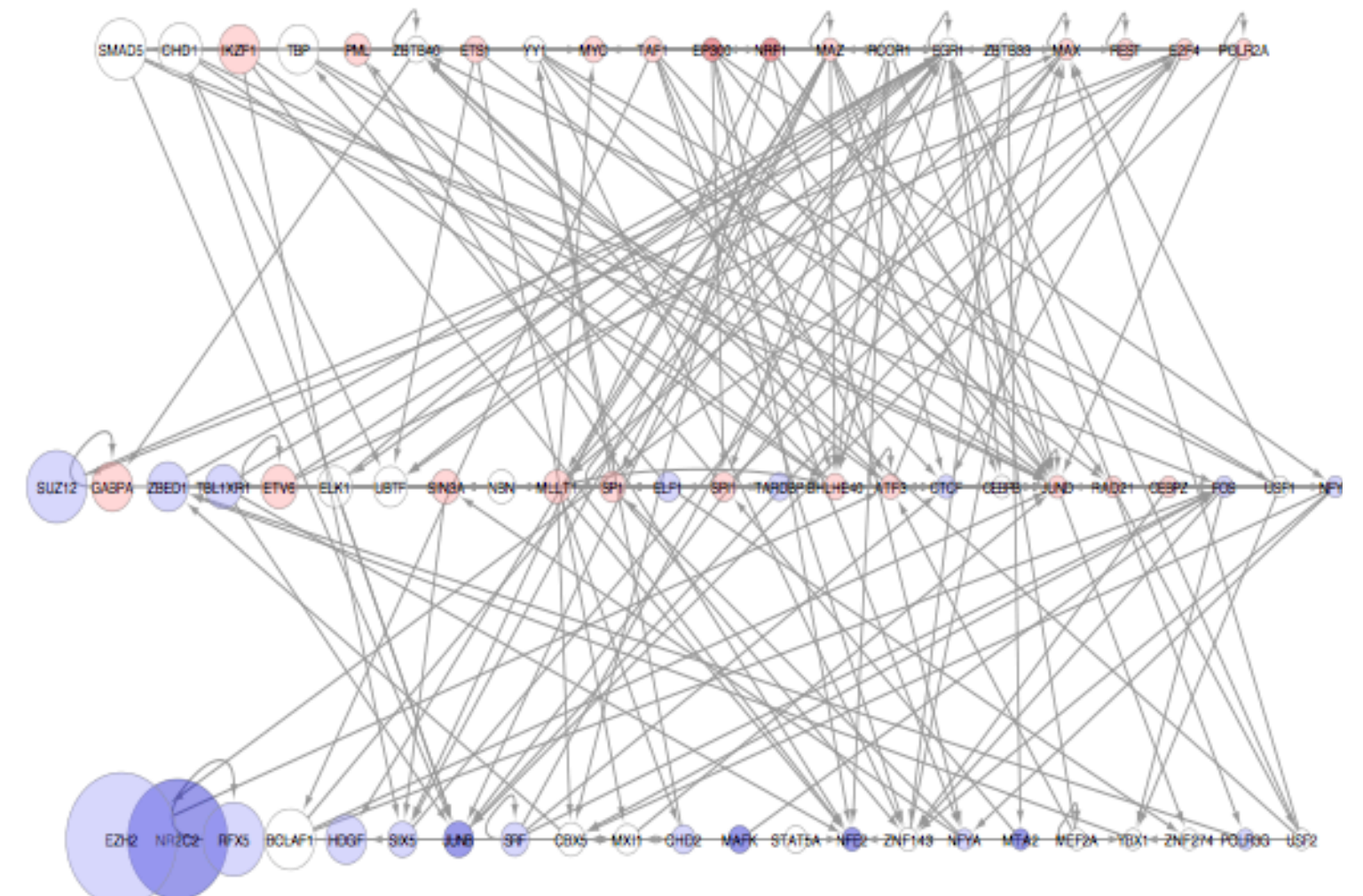


(d)

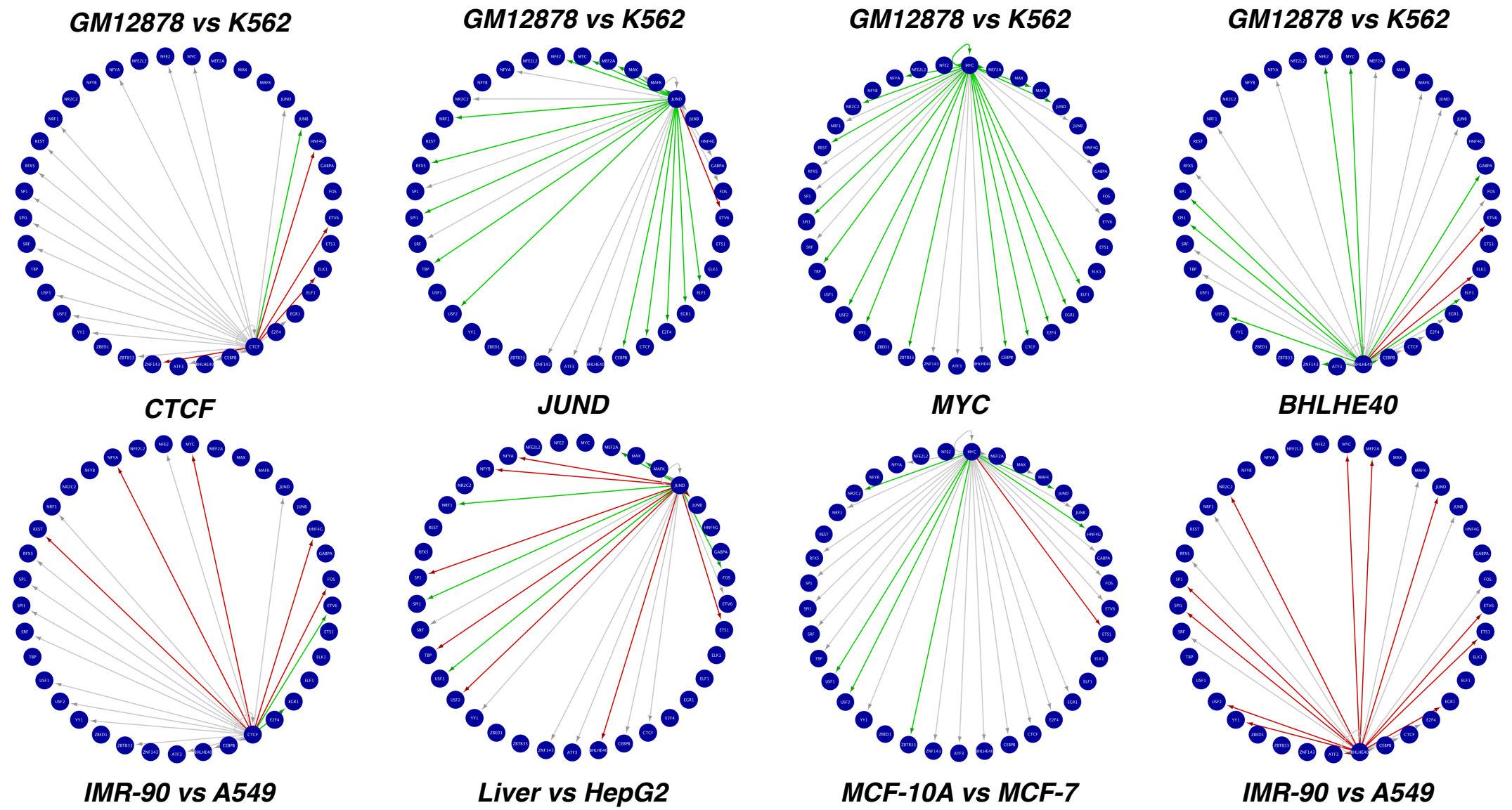
0.272

0.170

0.125

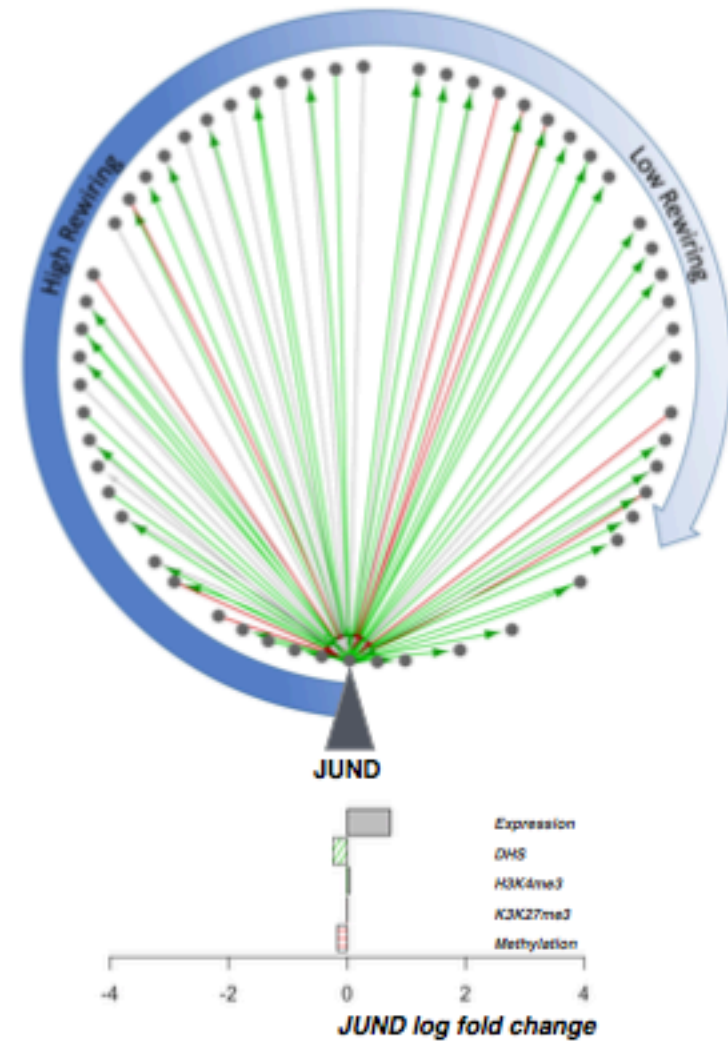


(e)

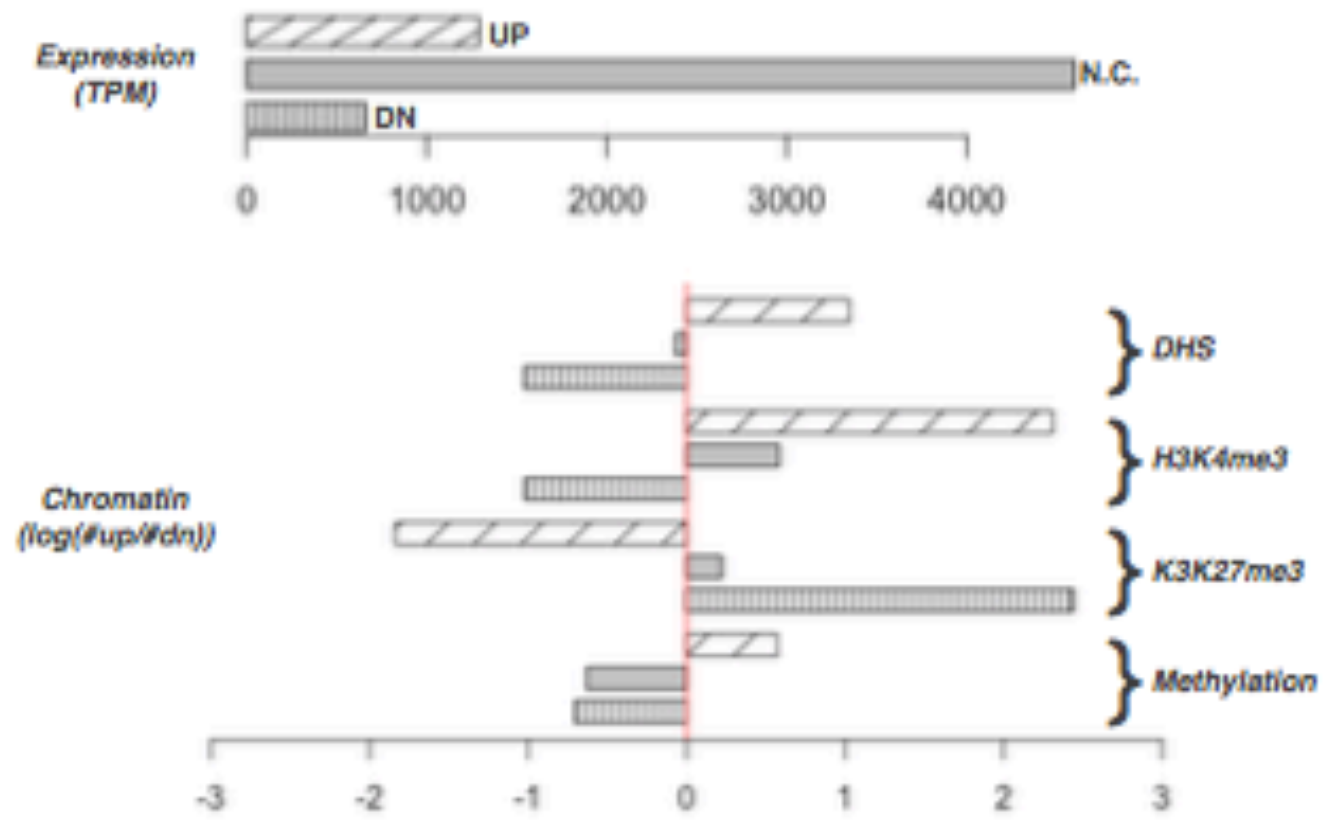


Overall Gene Target (n=15,189)

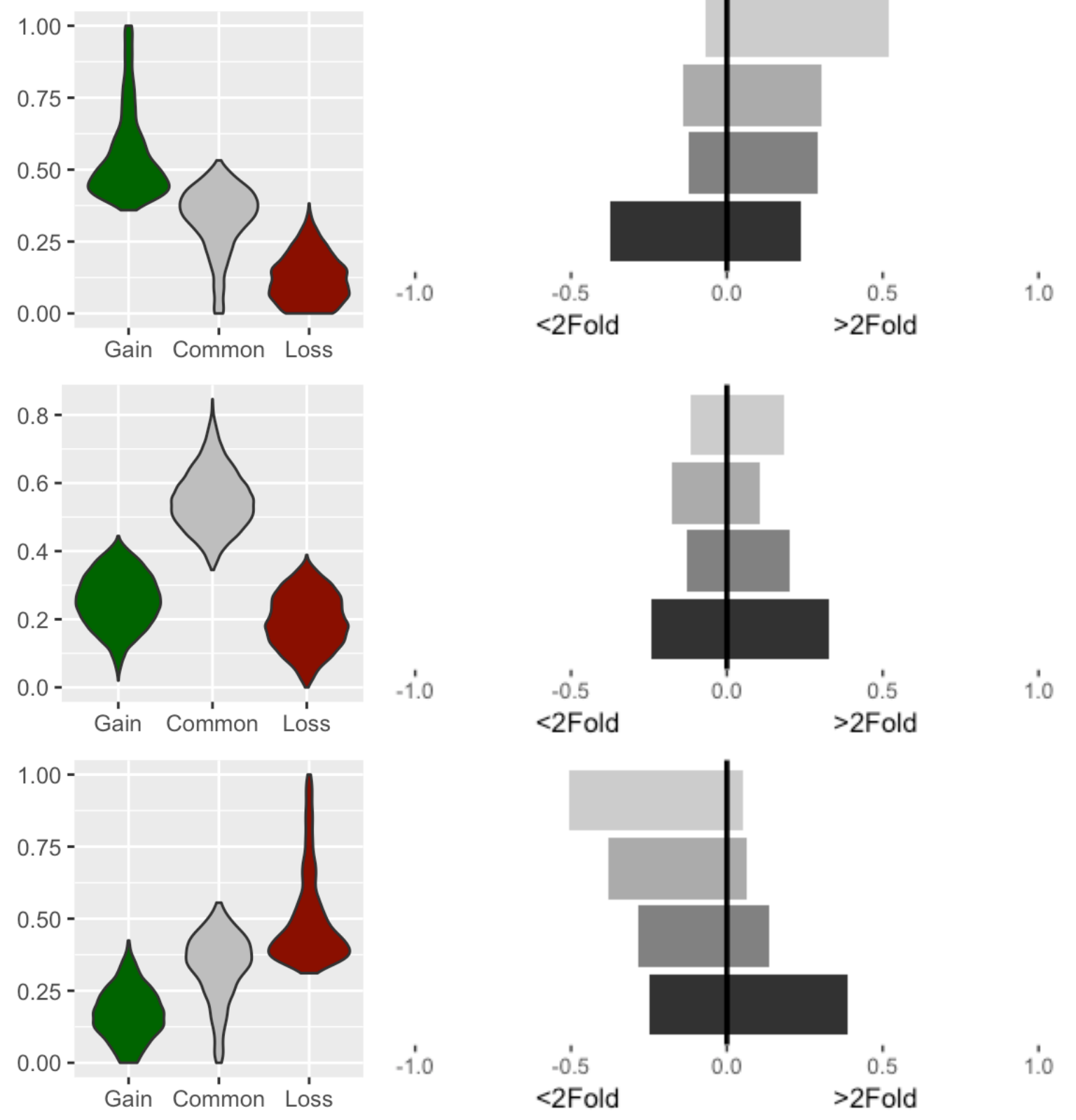
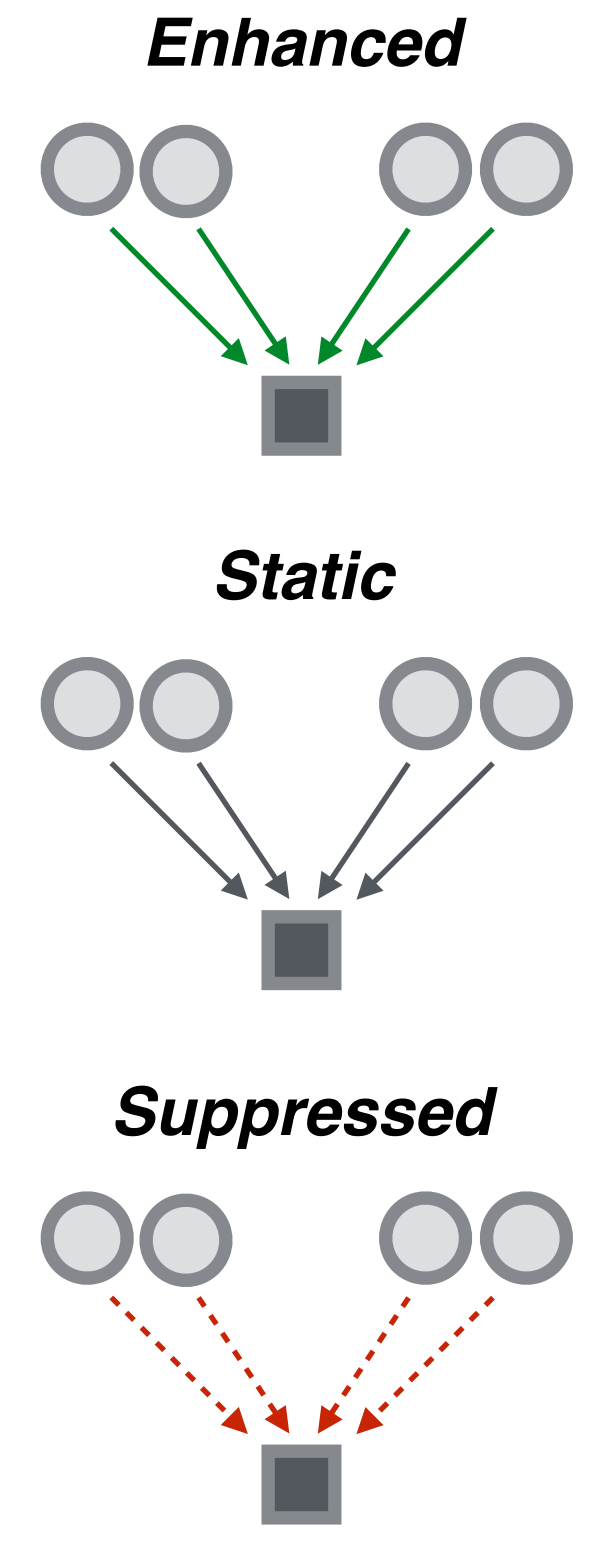
Expression (TPM)	UP			NC			DN		
n	2442			10294			2453		
%	16.1%			67.8%			16.1%		
DHS (TSS Cov) active	UP	NC	DN	UP	NC	DN	UP	NC	DN
n	622	1622	198	1280	7723	1291	108	1430	915
%	25.5%	66.4%	8.1%	12.4%	75.0%	12.5%	4.4%	58.3%	37.3%
H3K4me3 (TSS Cov) active promoter	UP	NC	DN	UP	NC	DN	UP	NC	DN
n	569	1817	56	801	8891	602	71	1753	629
%	23.3%	74.4%	2.3%	7.8%	86.4%	5.8%	2.9%	71.5%	25.6%
H3K27me3 (TSS Cov) inactive promoter	UP	NC	DN	UP	NC	DN	UP	NC	DN
n	25	2278	139	472	9446	376	237	2181	35
%	1.0%	93.3%	5.7%	4.6%	91.8%	3.7%	9.7%	88.9%	1.4%
Methylation (Sig Avg) repressive	UP	NC	DN	UP	NC	DN	UP	NC	DN
n	254	1994	194	741	8491	1062	117	2037	299
%	10.4%	81.7%	7.9%	7.2%	82.5%	10.3%	4.8%	83.0%	12.2%
Mutation ext.gene count	count > 1	has mut	no mut	count > 1	has mut	no mut	count > 1	has mut	no mut
	108	535	1907	402	2053	8241	117	548	1905
	4.4%	21.9%	78.1%	3.9%	19.9%	80.1%	4.8%	22.3%	77.7%
Mutation ext.gene pval < 0.05	29			138			57		
	1.2%			1.3%			2.3%		



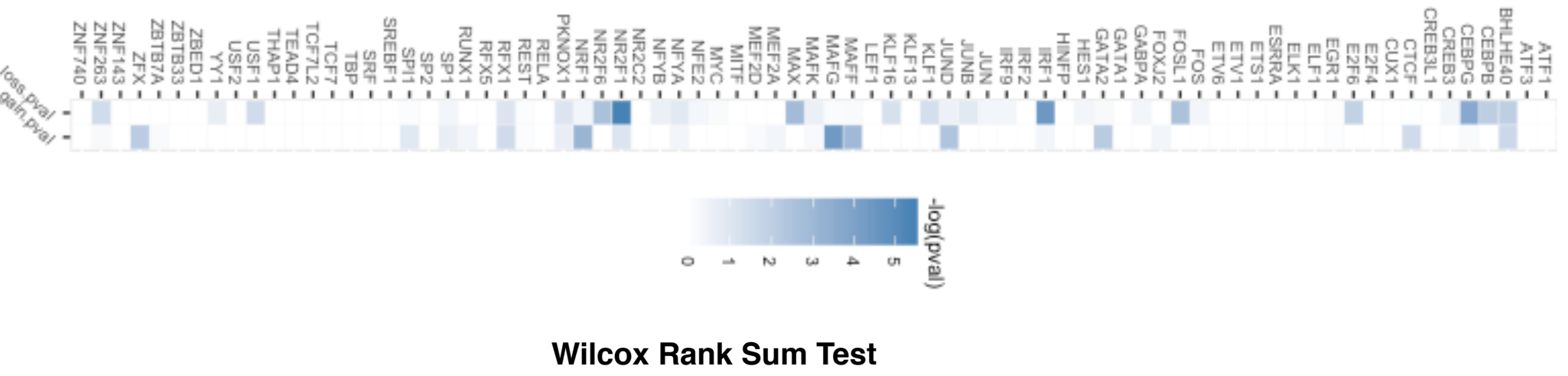
JUND Gained Targets



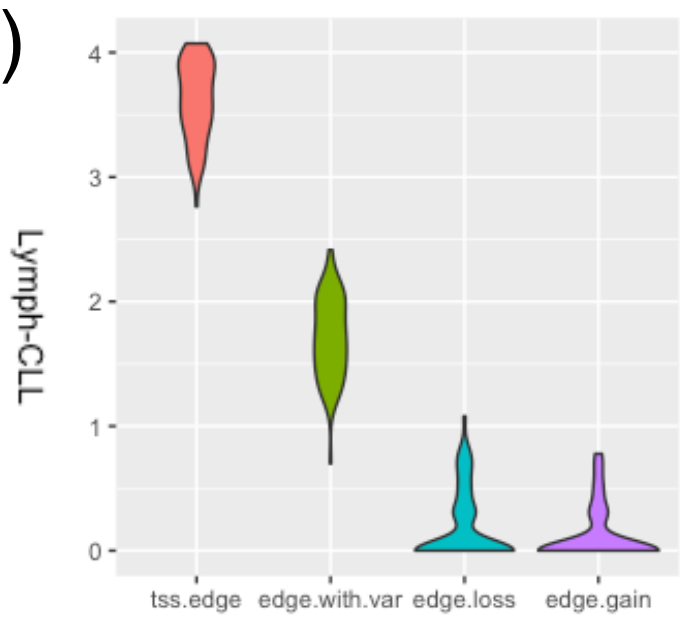
(a)



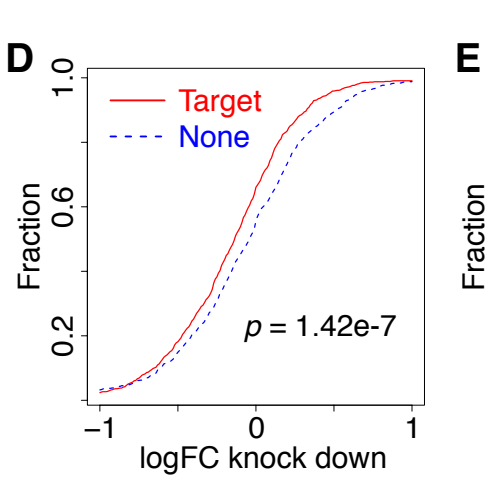
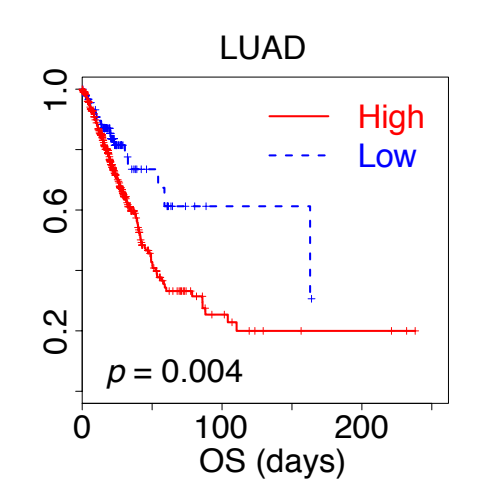
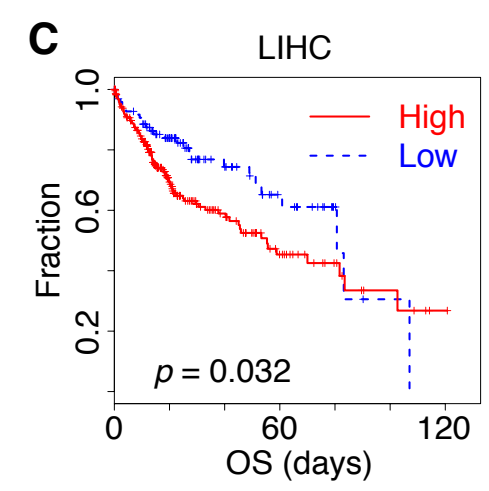
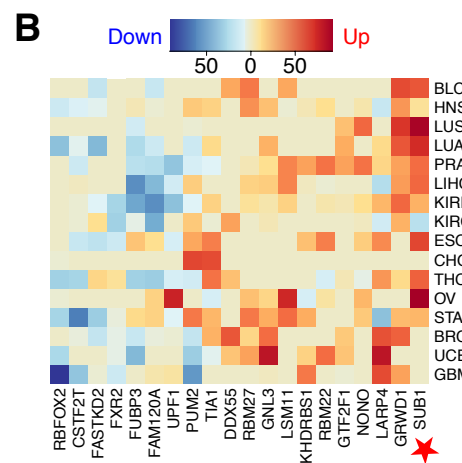
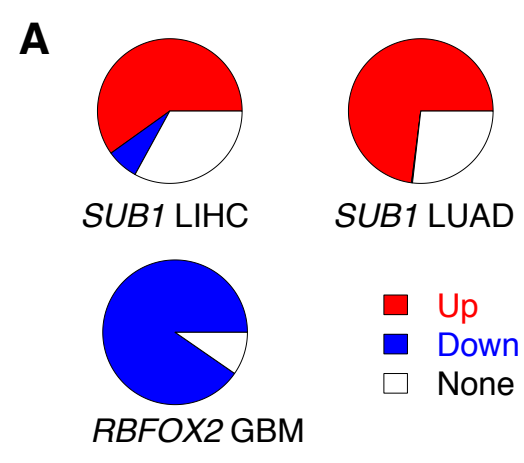
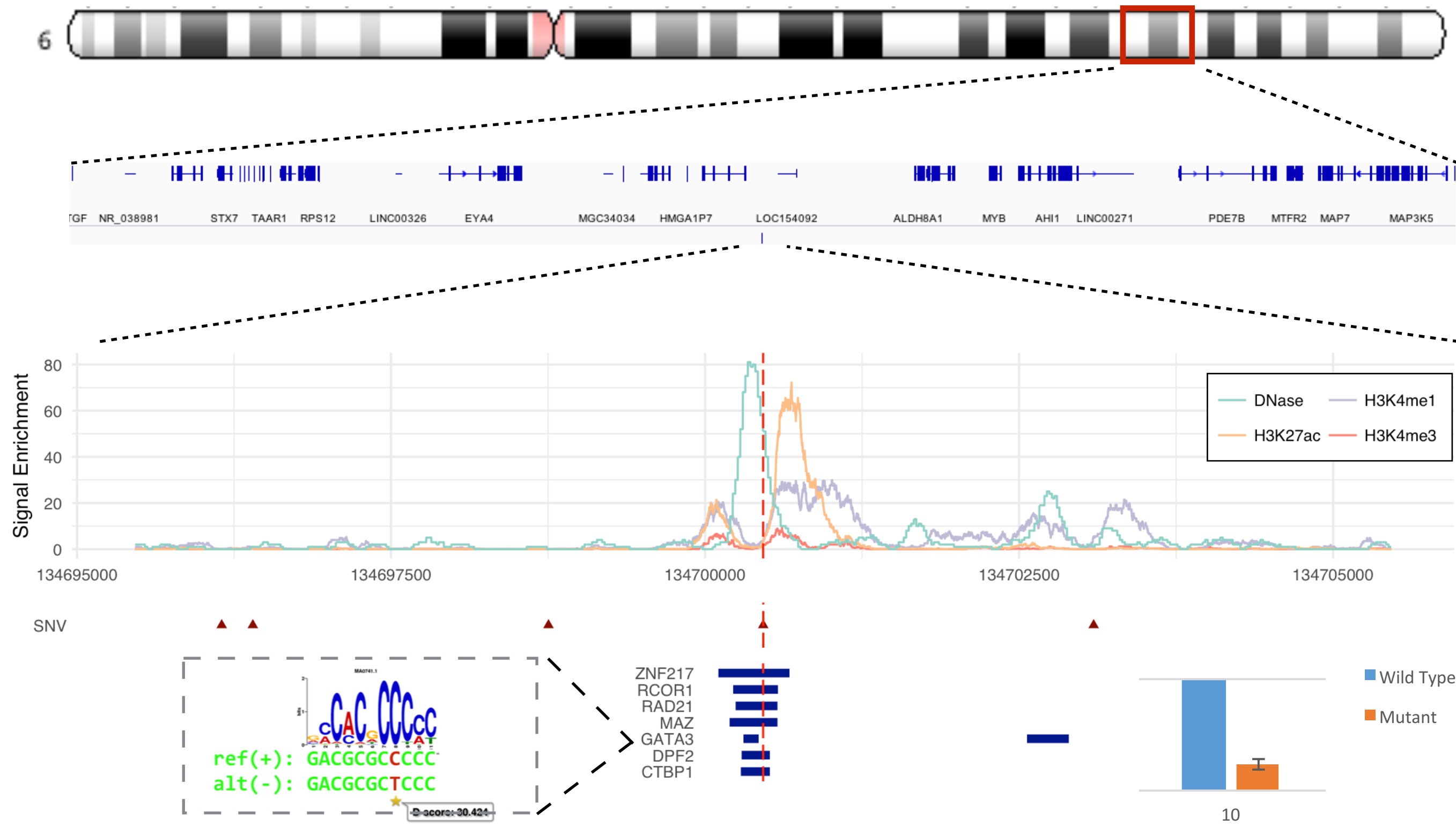
(b)

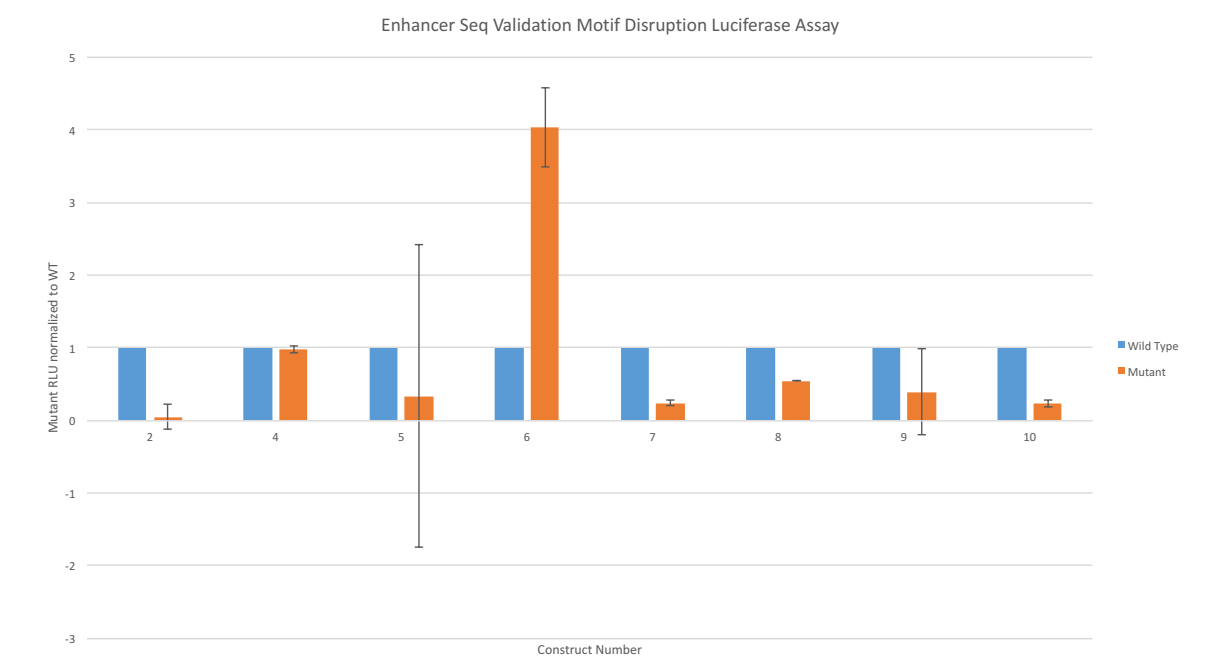


(c)

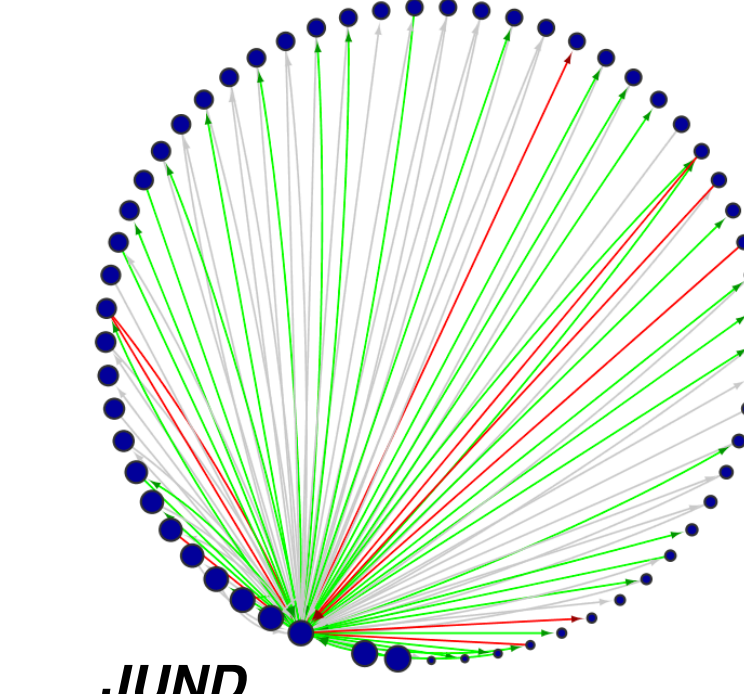
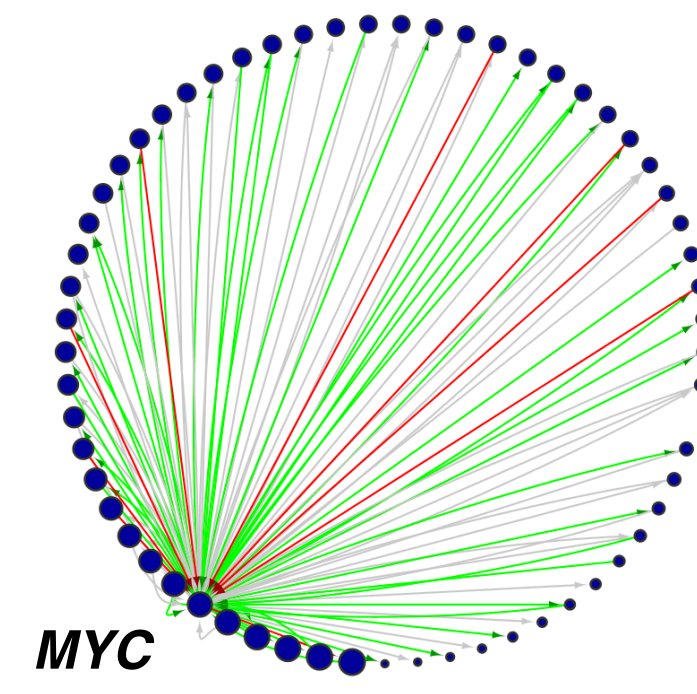
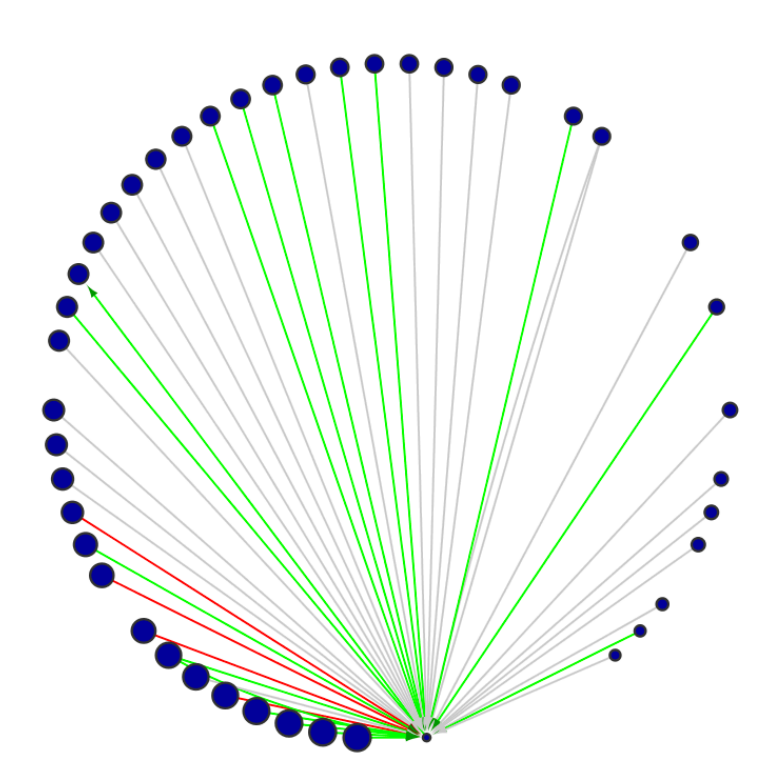
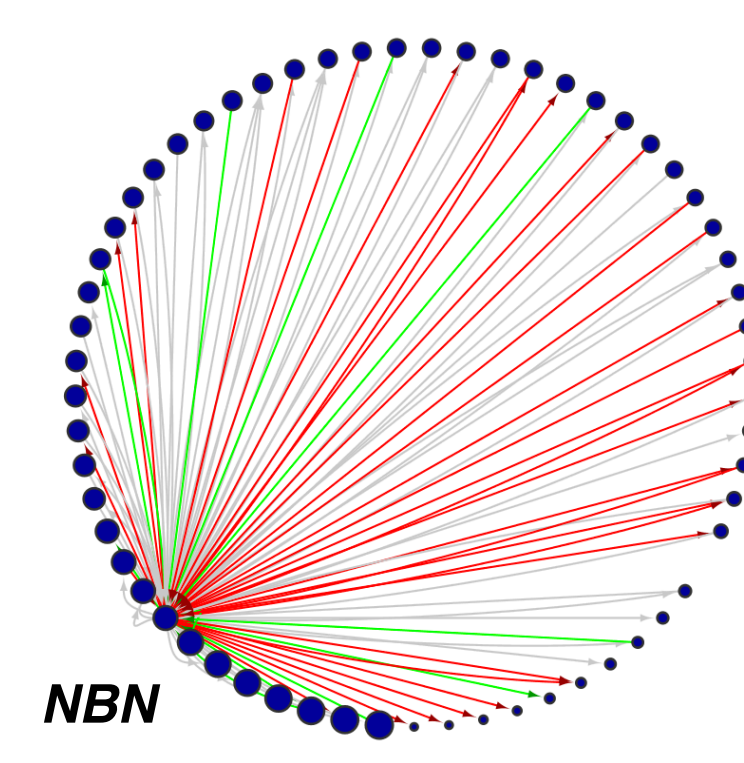
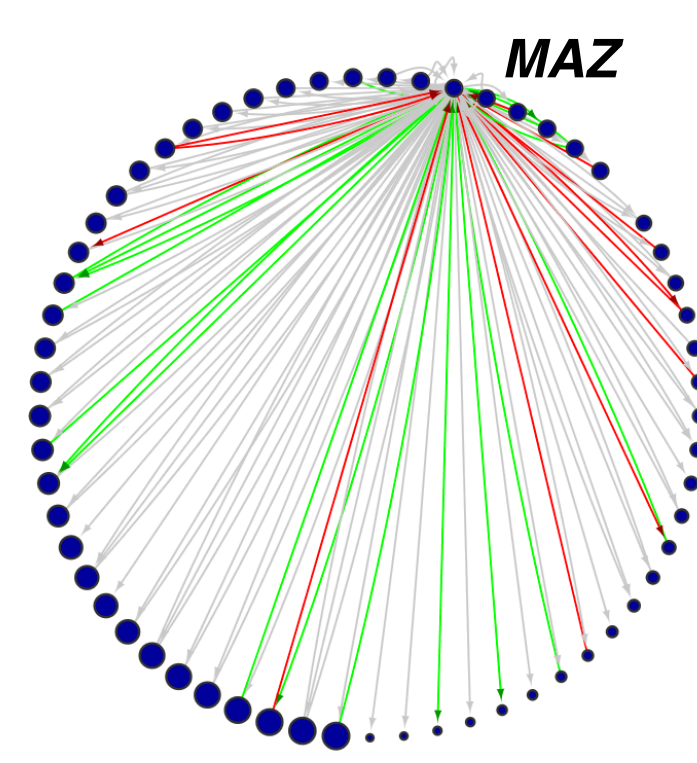


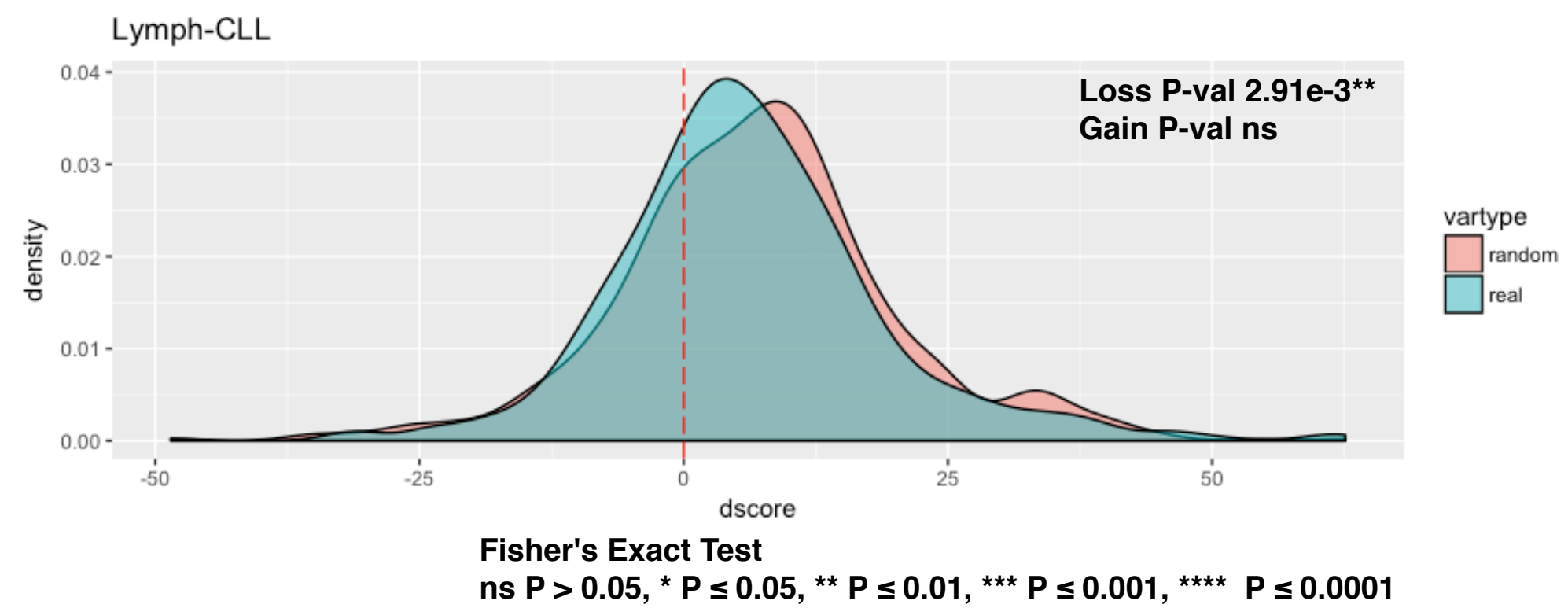
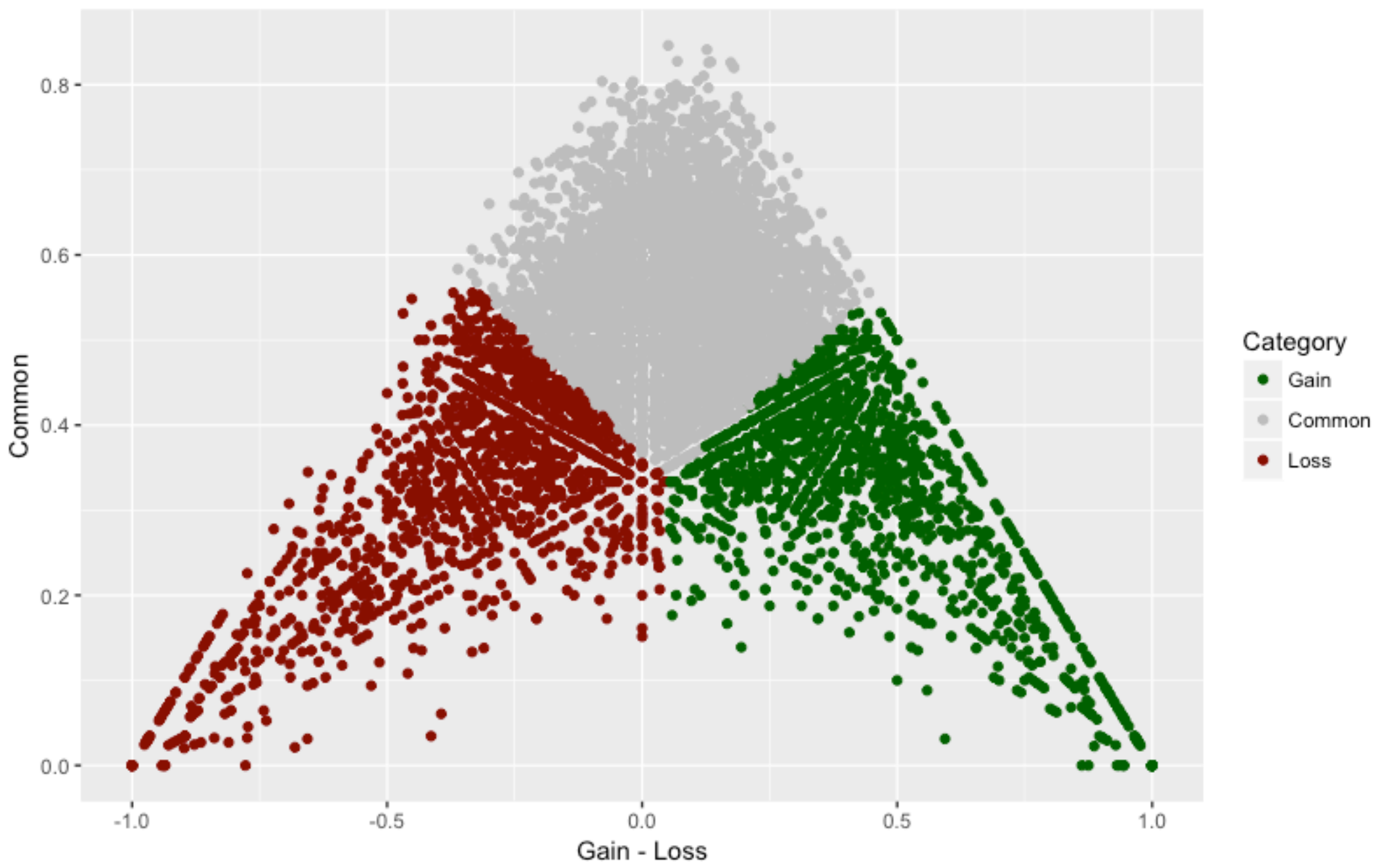
(a)



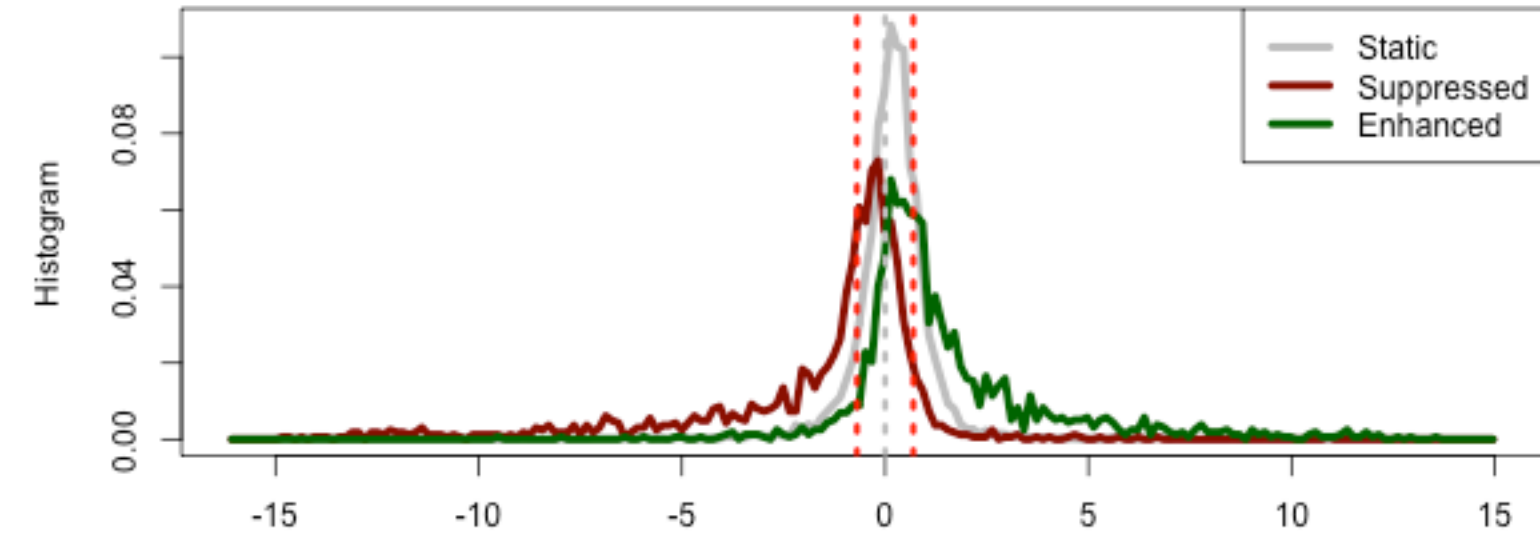


	Sample02	Sample04	Sample05	Sample06	Sample07	Sample08	Sample09	Sample10
chr	chr21	chr17	chr20	chr7	chr20	chr7	chr7	chr6
pos	27,541,982	38,474,408	43,971,343	1,598,567	58,563,412	150,759,483	5,596,005	134,700,462
ref	G	C	G	C	C	C	T	G
alt	A	G	C	T	T	G	G	T
D-score_min	20.361	16.910	3.665	15.746	7.217	13.959	13.372	13.989
D-score_mean	20.361	16.910	15.834	15.746	15.521	15.242	15.019	14.591
D-score_max	20.361	16.910	30.424	15.746	21.648	17.325	17.993	15.796

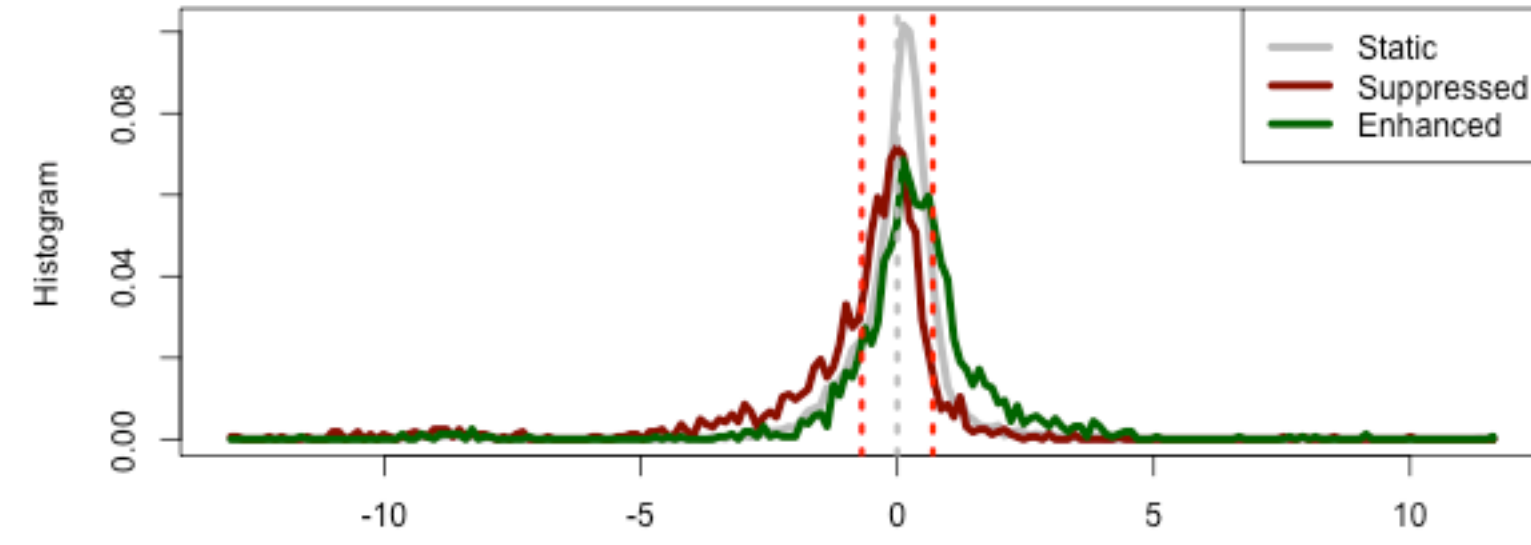




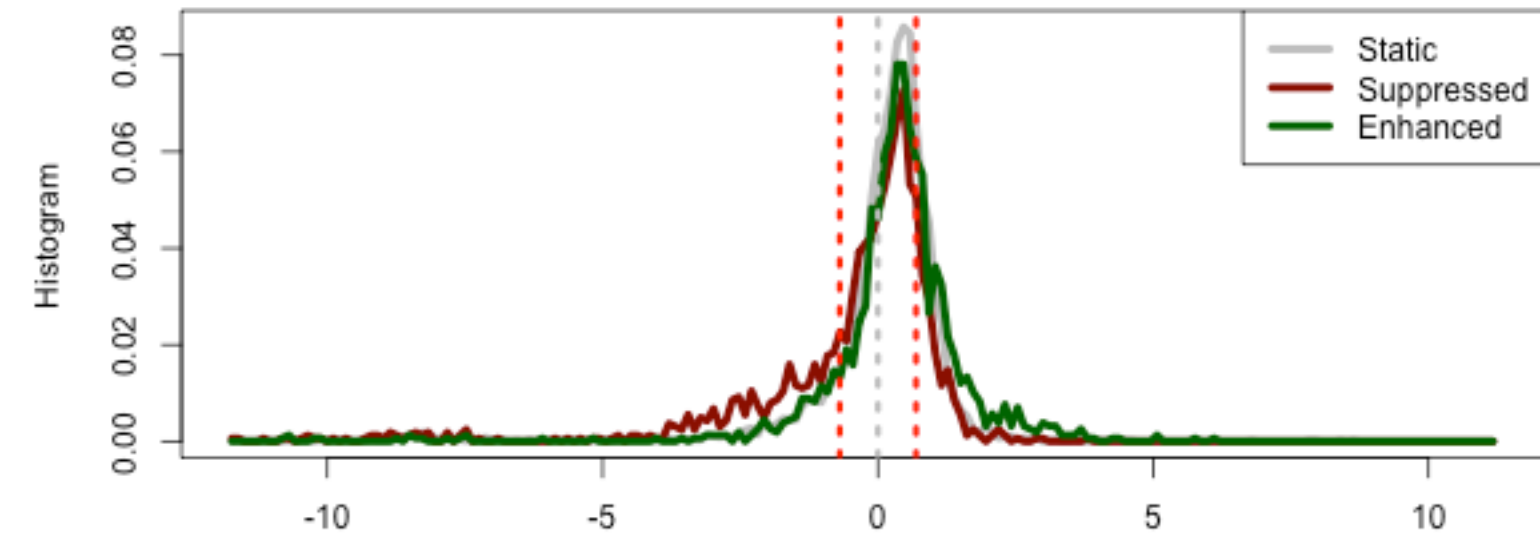
Expression(TPM) log(fc)



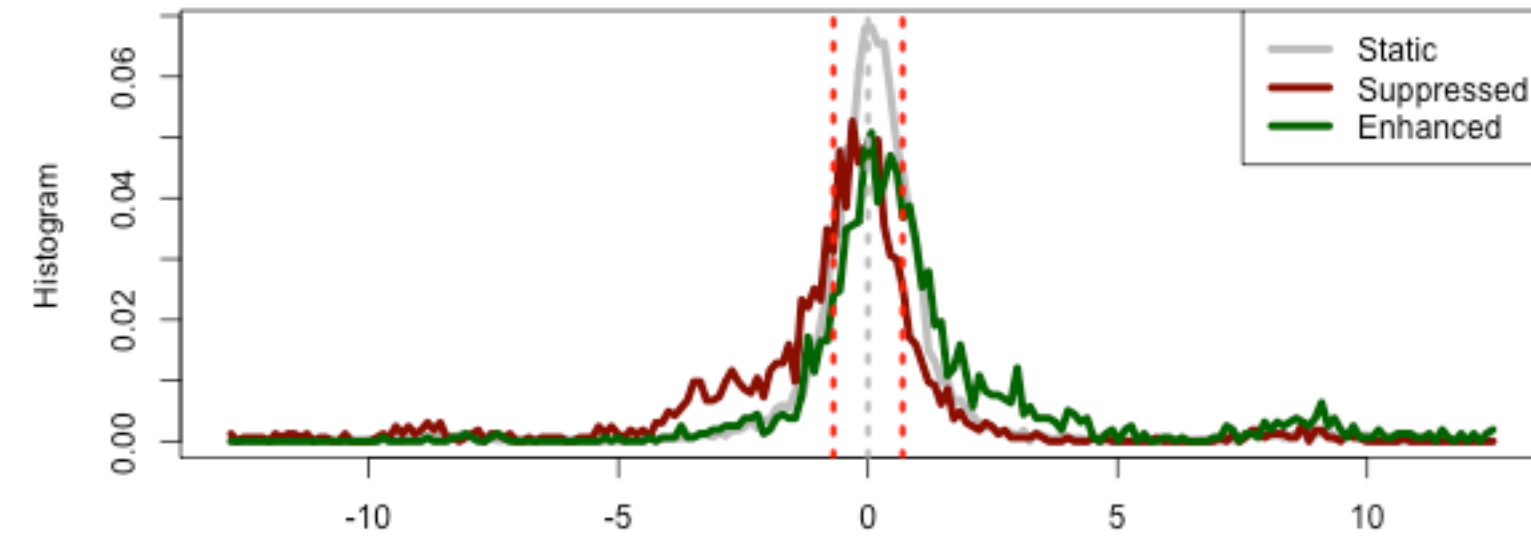
DNase I log(fc)



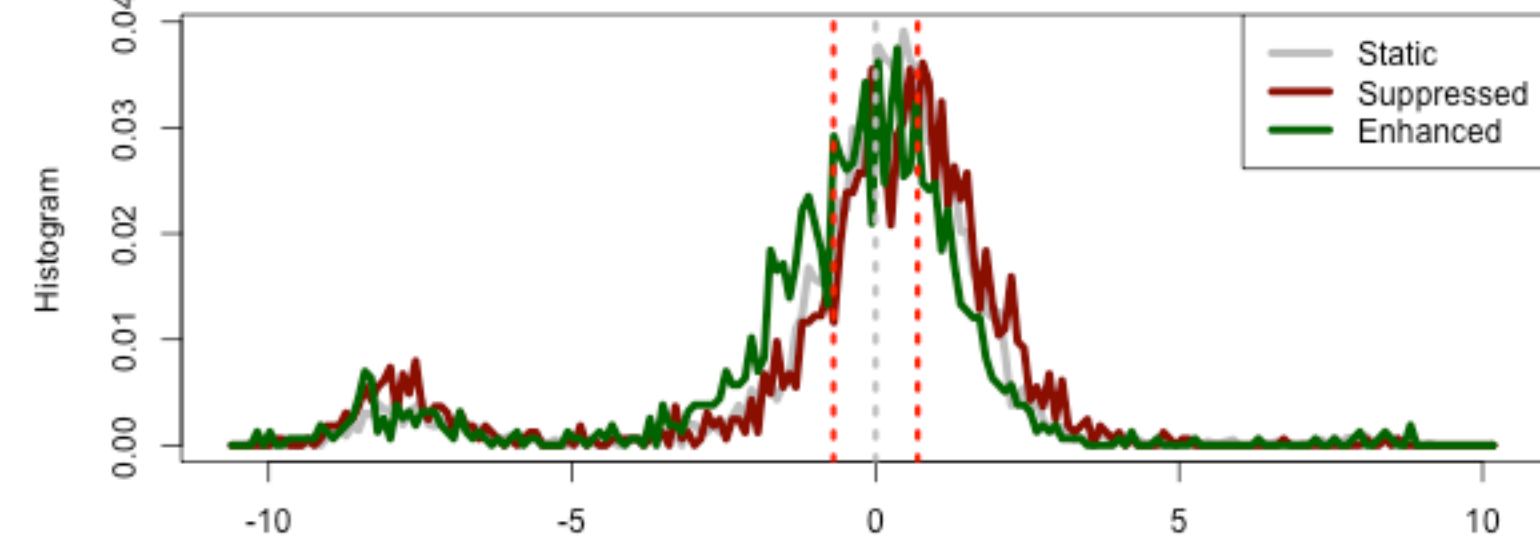
H3K4me3 log(fc)



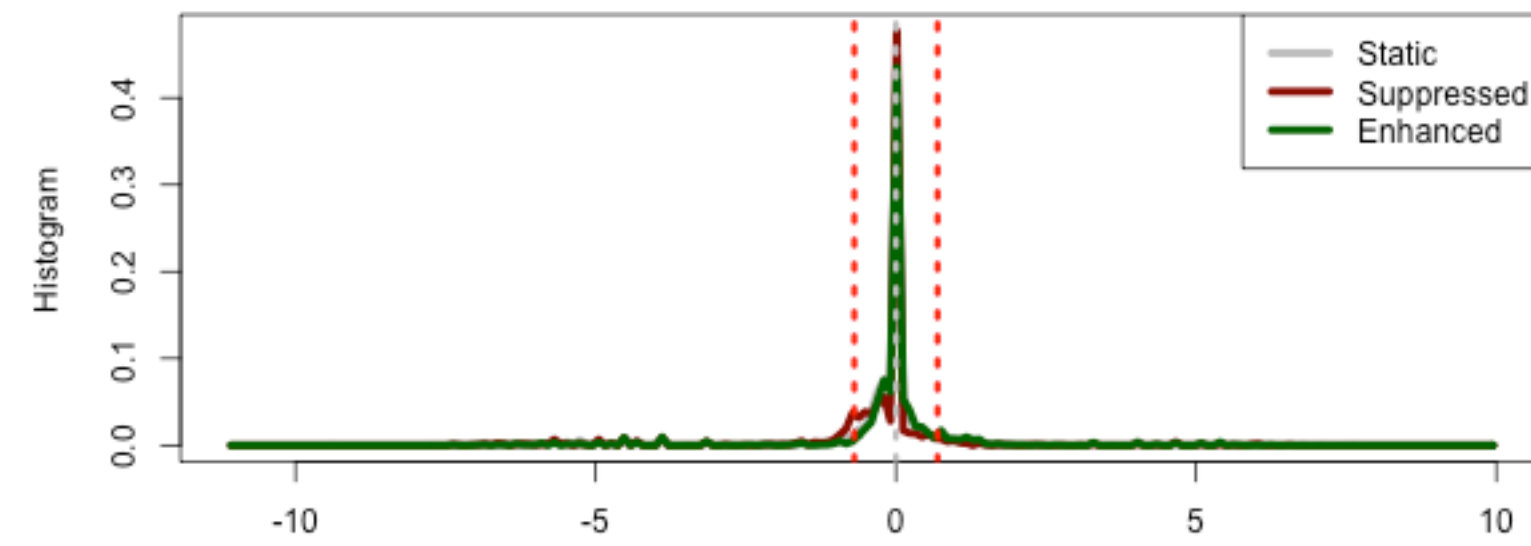
H3K27ac log(fc)



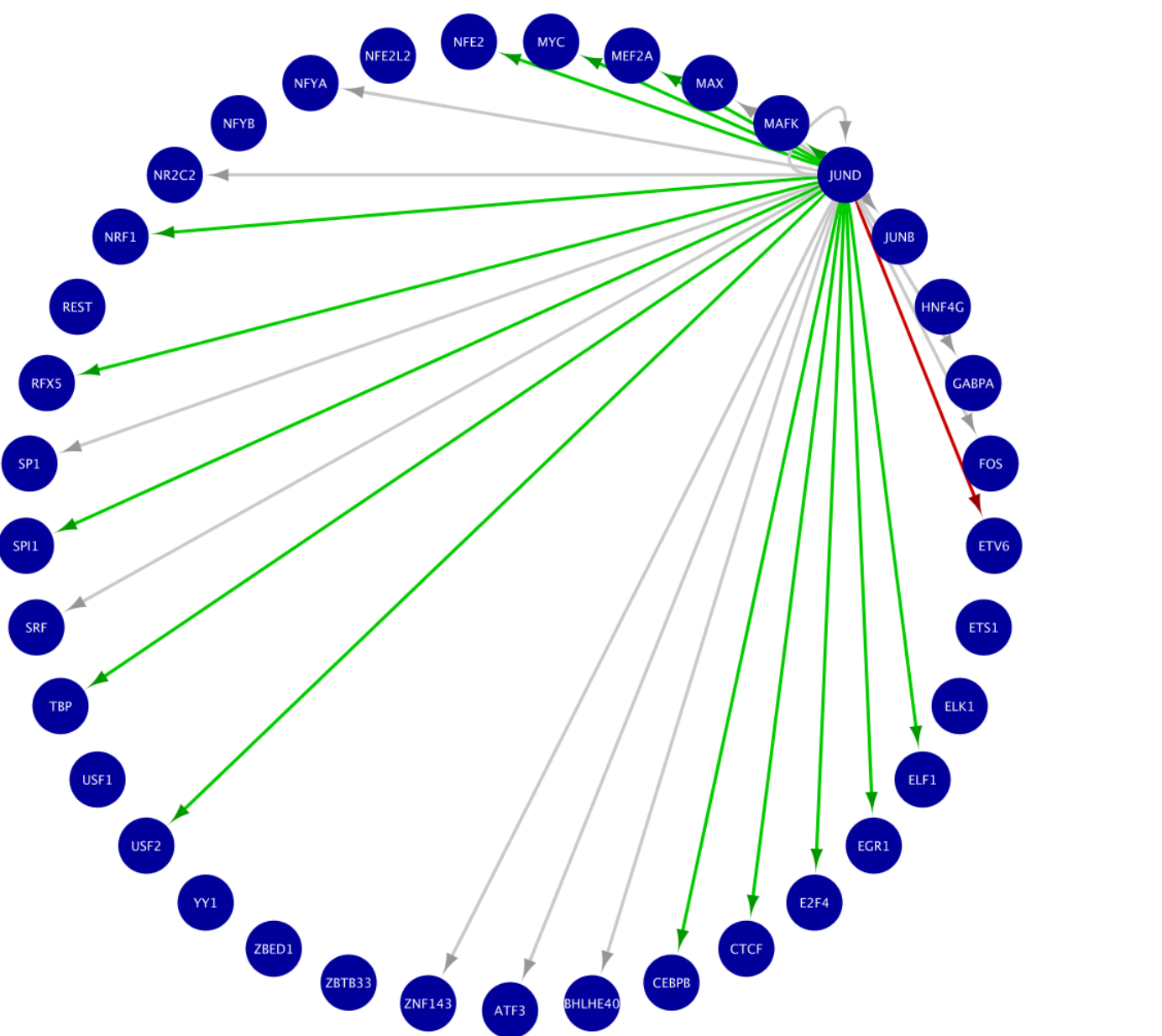
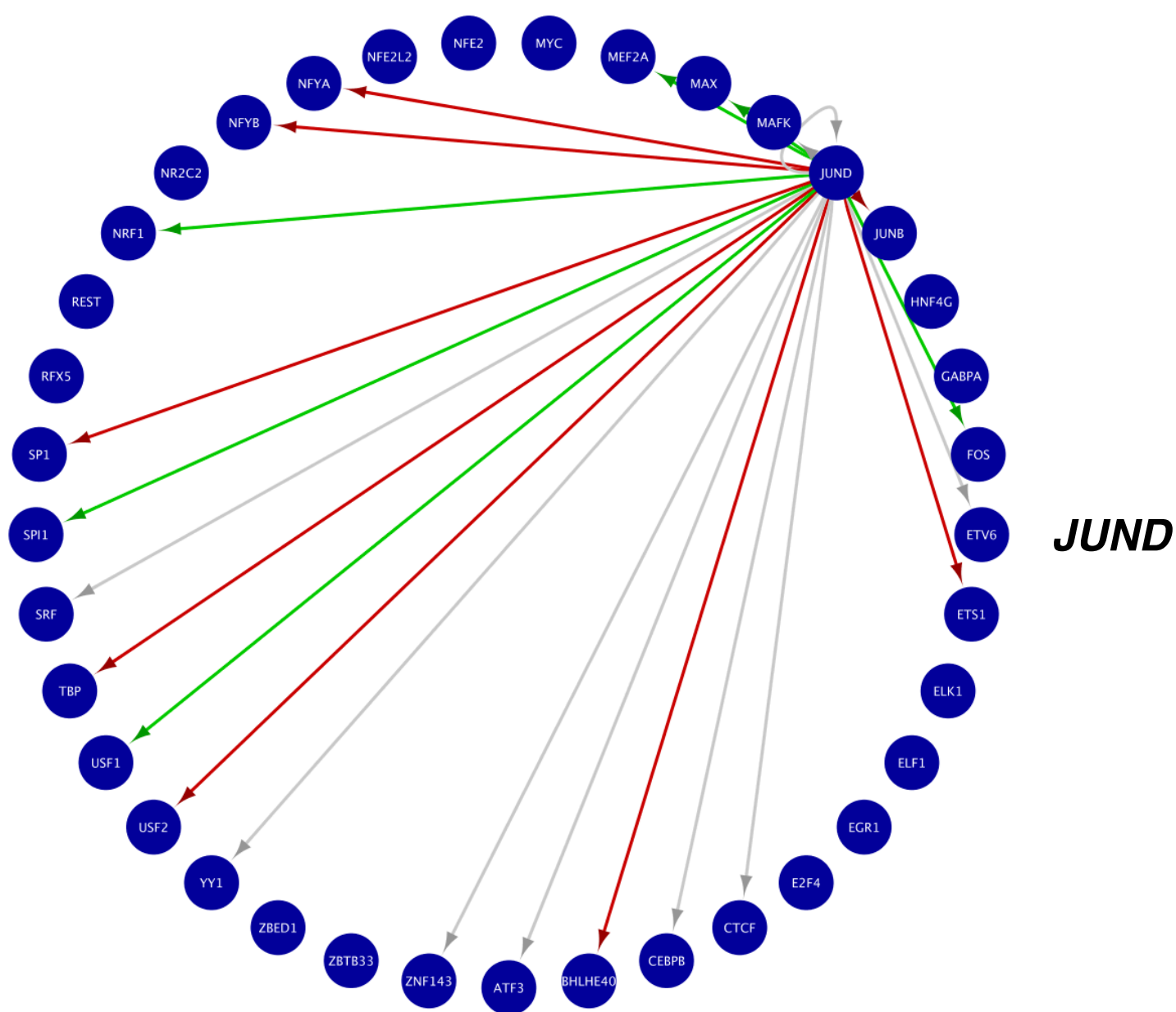
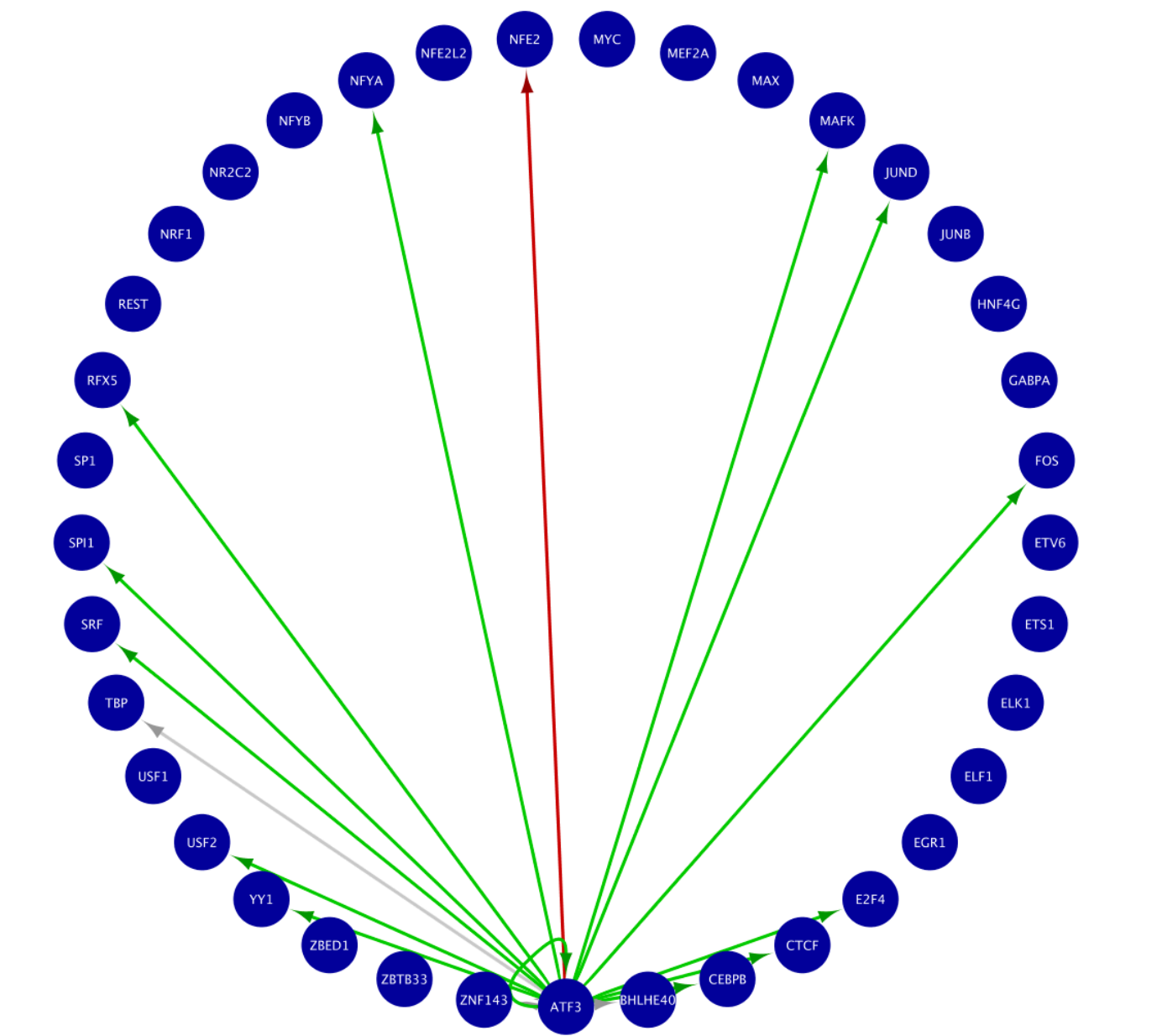
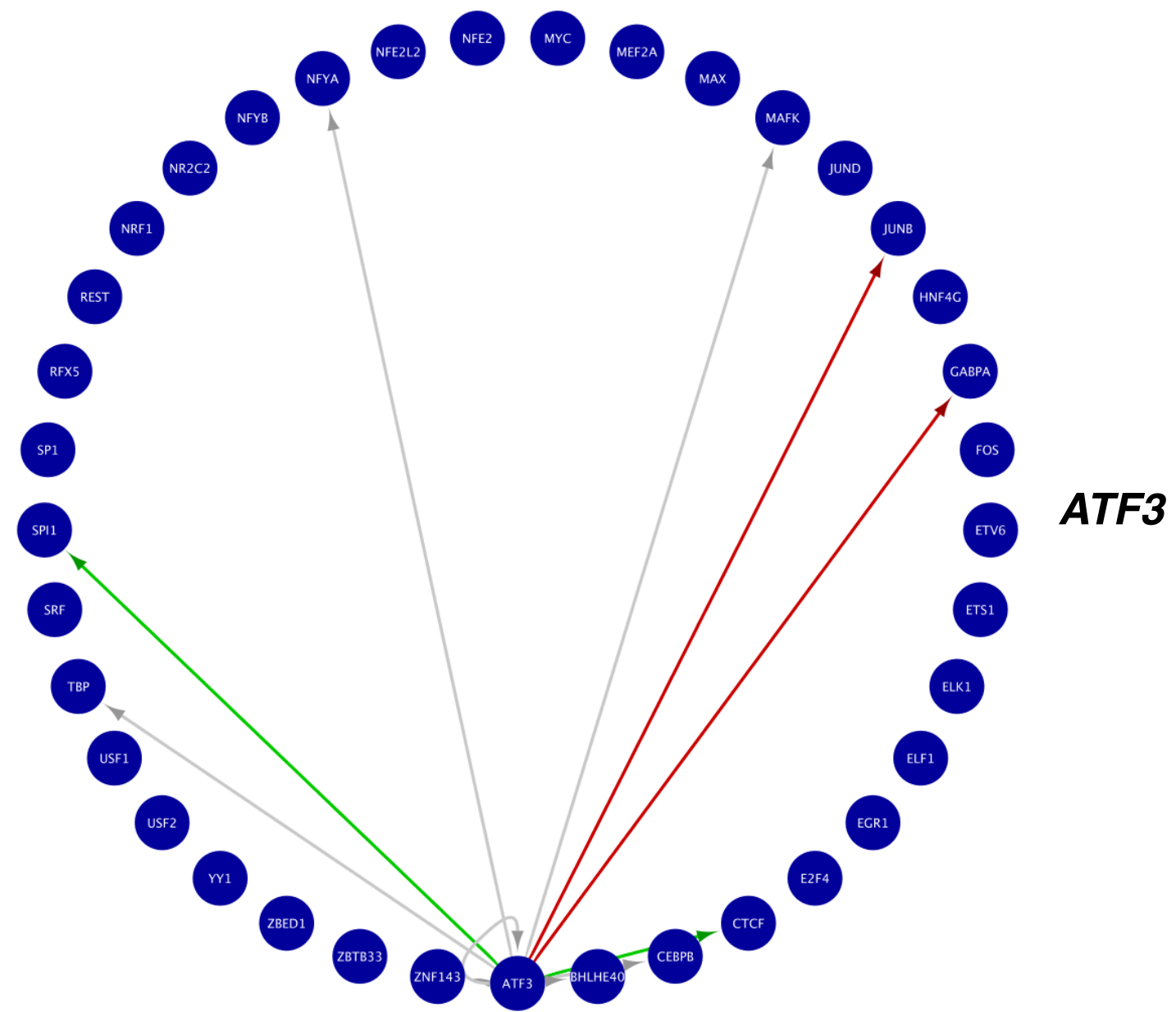
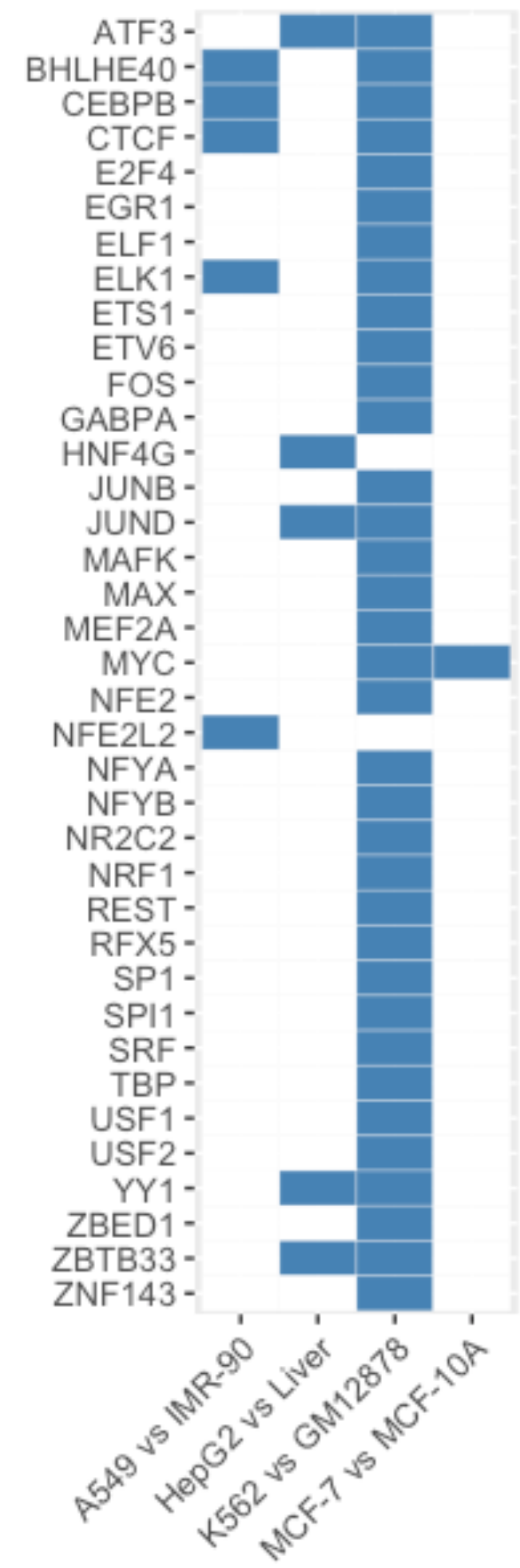
H3K27me3 log(fc)

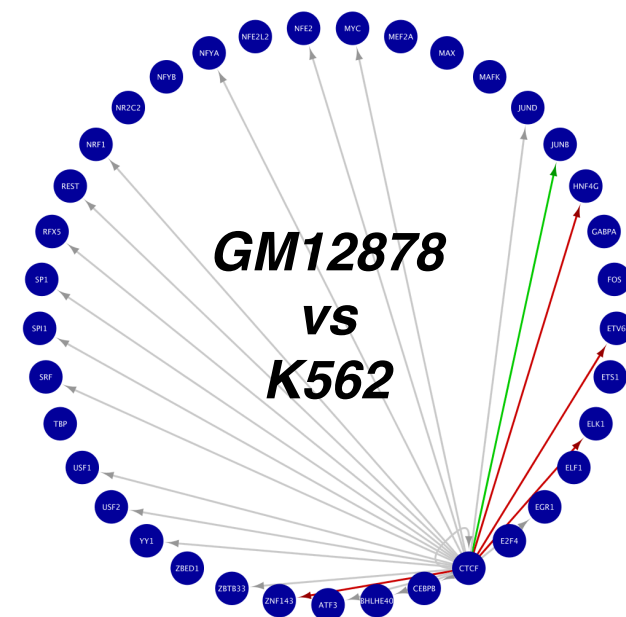


5mC log(fc)

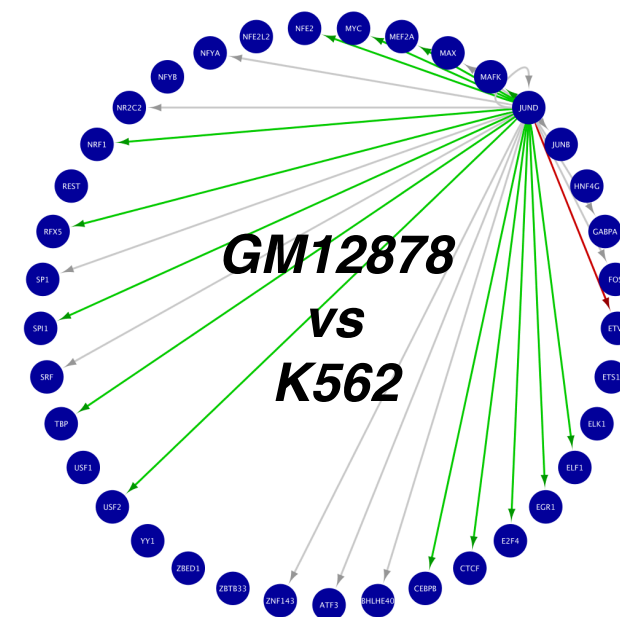


Cross-Cancer TFSS Matrix

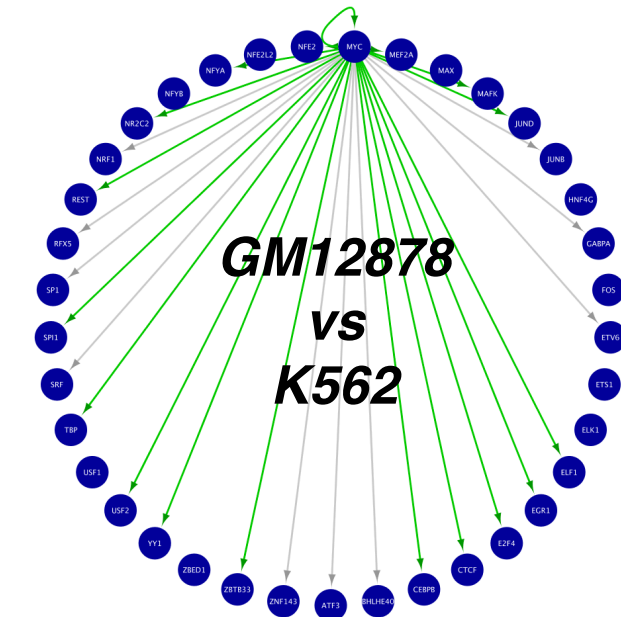




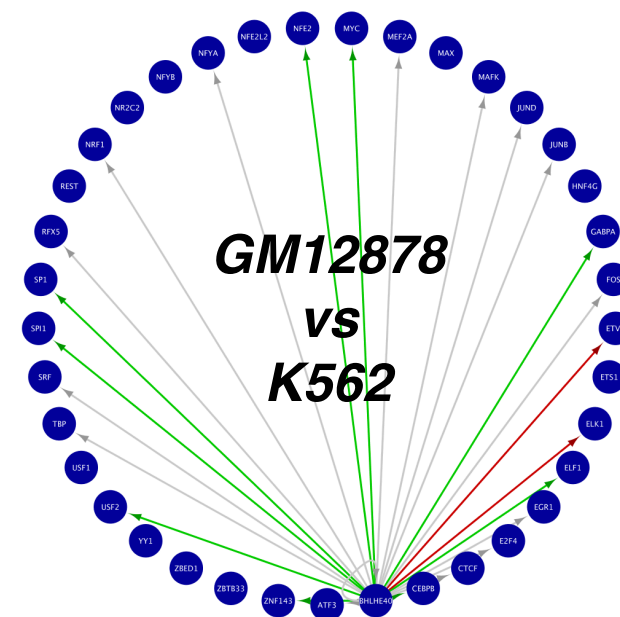
CTCF



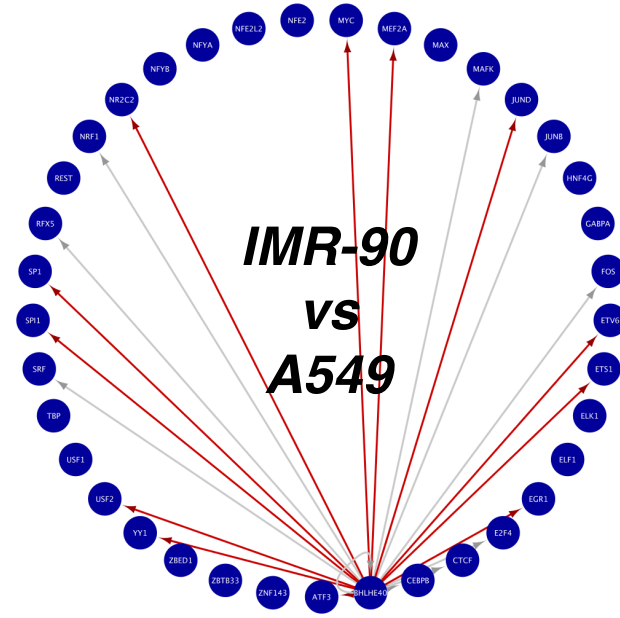
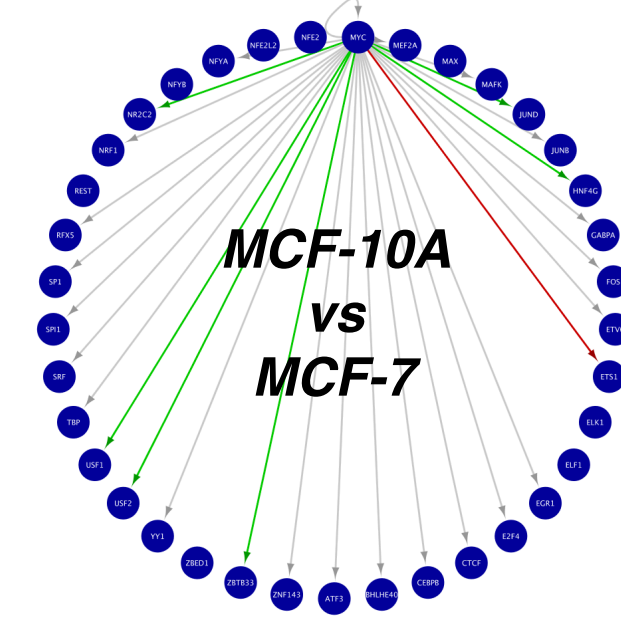
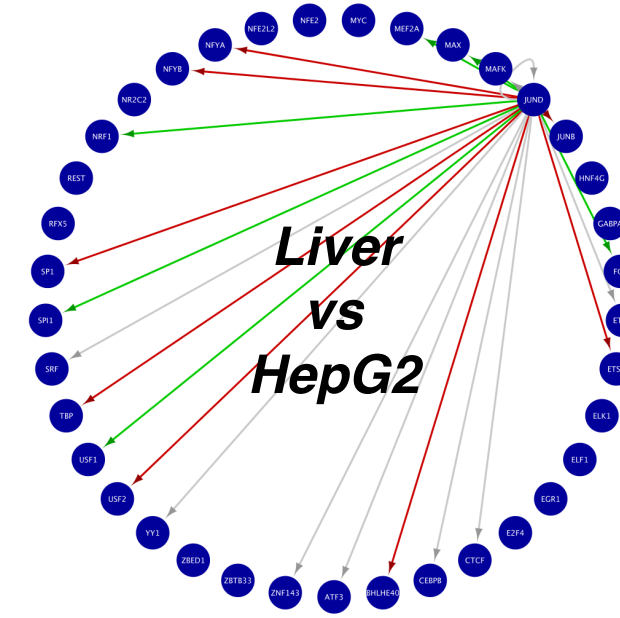
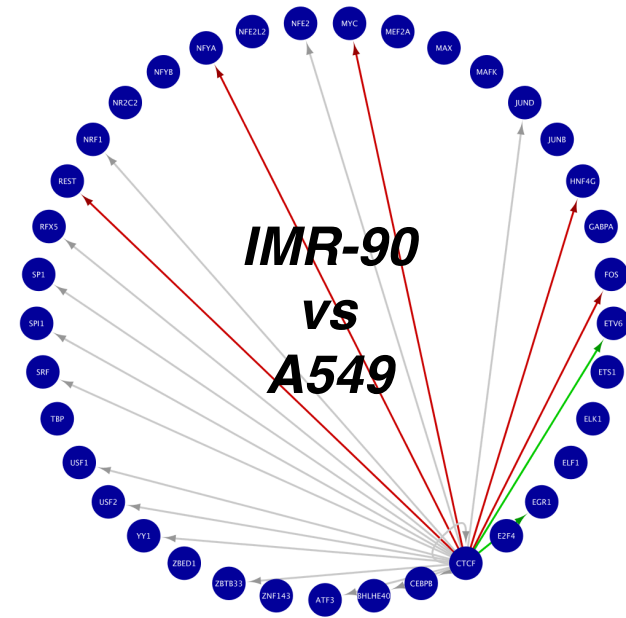
JUND

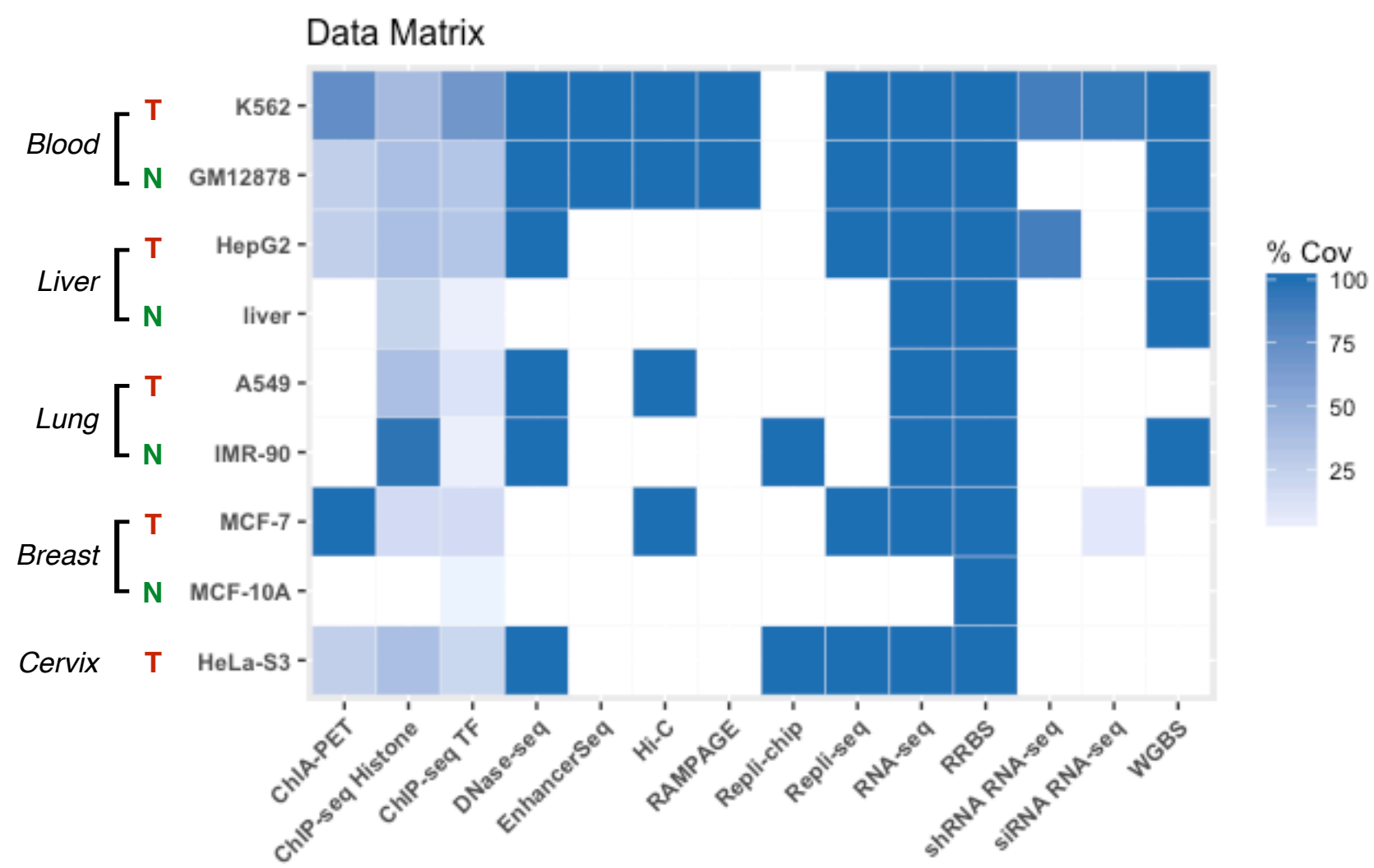


MYC



BHLHE40





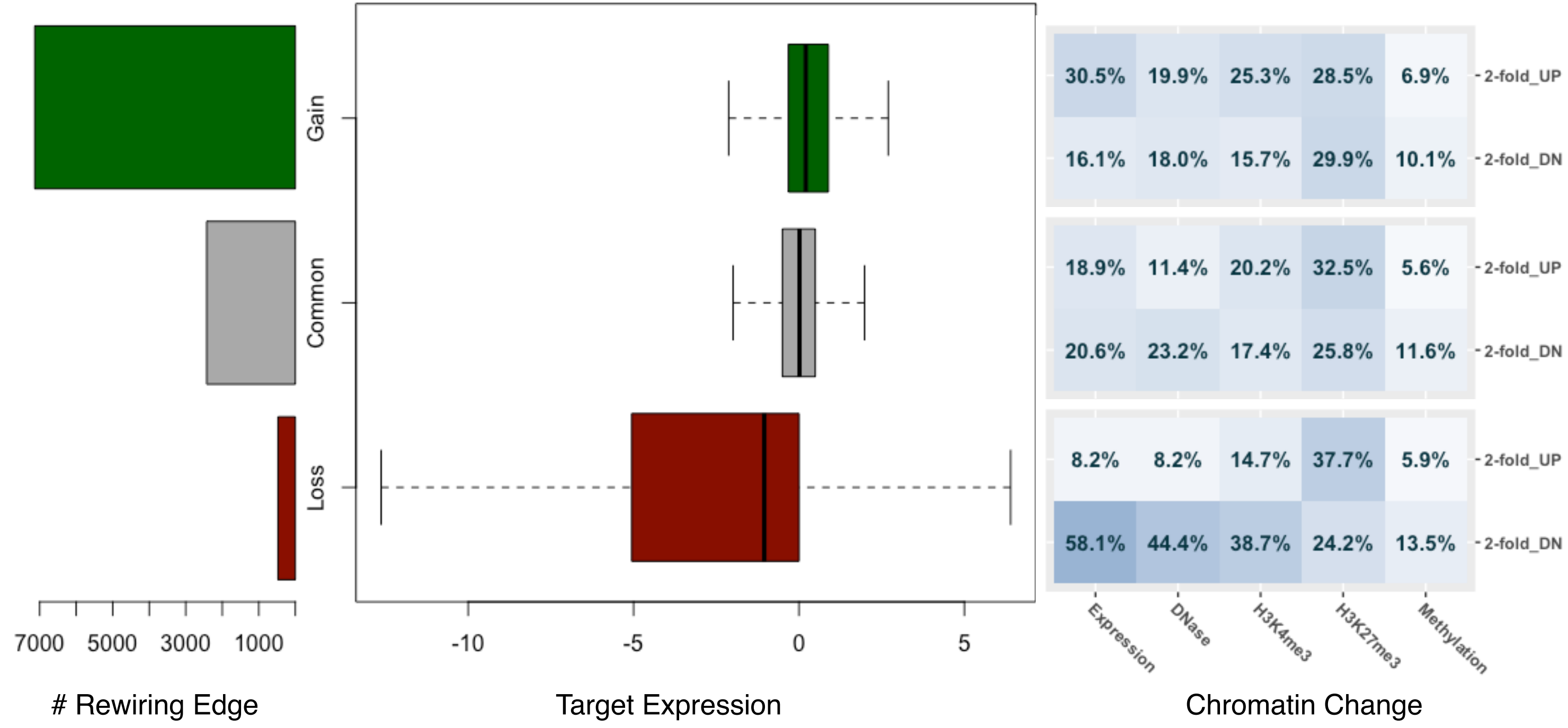
Data Matrix

Blood	T K562	209	64	17	1	12	1	1	1	1	3	1	0	1	219	29	1	1	1
	N GM12878	101	50	6	1	11	1	1	1	1	1	1	0	1	0	0	1	0	0
Liver	T HepG2	97	48	7	1	11	1	0	1	1	1	0	0	1	221	0	0	0	0
	N liver	7	5	0	0	7	1	0	1	1	0	0	0	0	0	0	0	0	0
Lung	T A549	32	21	3	1	11	1	0	1	0	0	1	0	0	0	0	0	0	0
	N IMR-90	9	6	1	1	28	1	0	1	1	0	0	1	0	0	0	0	0	0
Breast	T MCF-7	52	15	3	0	5	1	0	1	0	4	1	0	1	0	2	0	1	1
	N MCF-10A	4	3	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Cervix	T HeLa-S3	60	29	4	1	11	1	0	1	0	1	0	1	0	0	0	0	0	0

Data Matrix

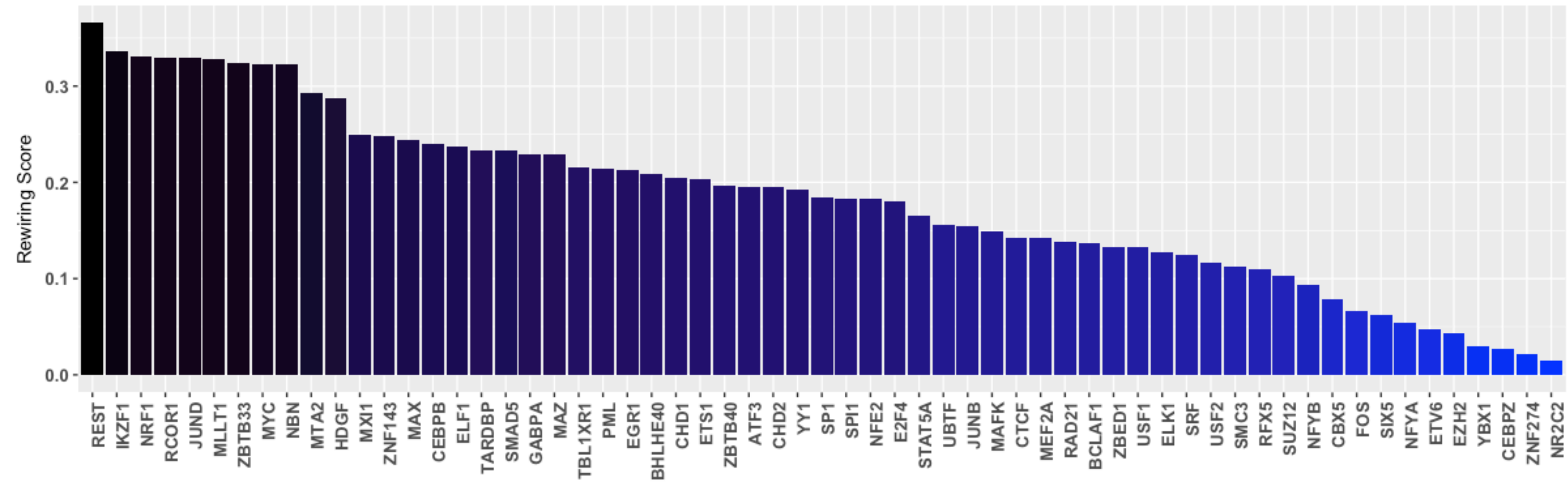
Blood	T K562	209	64	17	1	12	1	1	1	1	3	1	0	1	219	29	1	1	1	95
	N GM12878	101	50	6	1	11	1	1	1	1	1	1	0	1	0	0	1	1	1	0
Liver	T HepG2	97	48	7	1	11	1	0	1	1	1	0	0	1	221	0	0	0	0	327
	N liver	7	5	0	0	7	1	0	1	1	0	0	0	0	0	0	0	0	0	0
Lung	T A549	32	21	3	1	11	1	0	1	0	0	1	0	0	0	0	0	0	0	38
	N IMR-90	9	6	1	1	28	1	0	1	1	0	0	1	0	0	0	0	0	0	0
Breast	T MCF-7	52	15	3	0	5	1	0	1	0	4	1	0	1	0	2	0	1	1	198
	N MCF-10A	4	3	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Cervix	T HeLa-S3	60	29	4	1	11	1	0	1	0	1	0	1	0	0	0	0	0	0	2

JUND

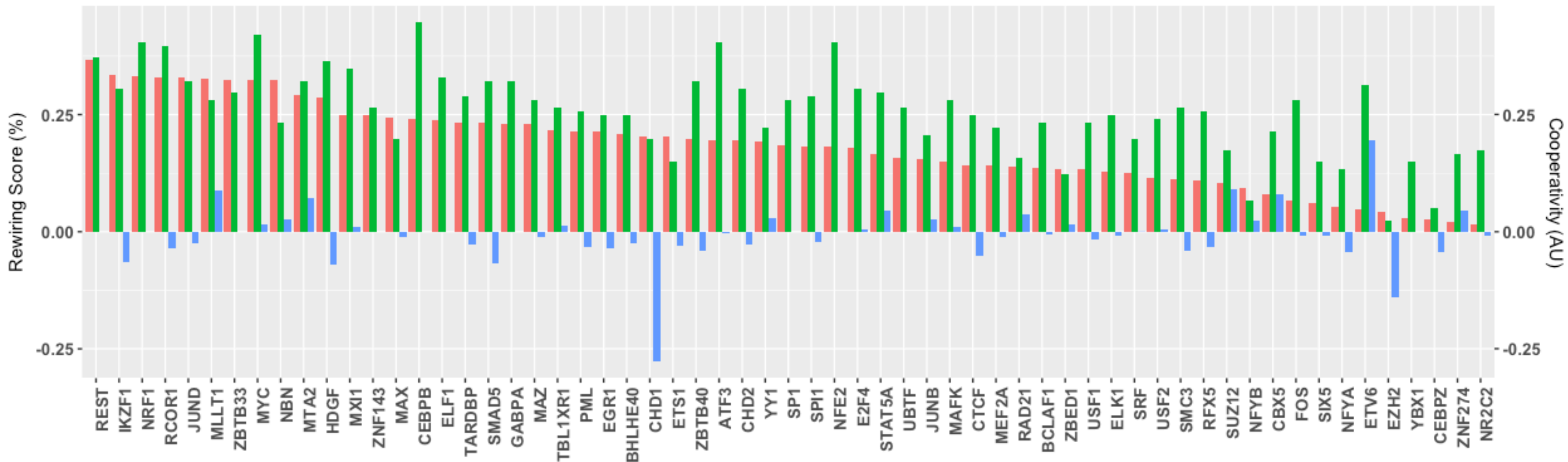


new TSS network, one TSS per gene

TF-GENE Network

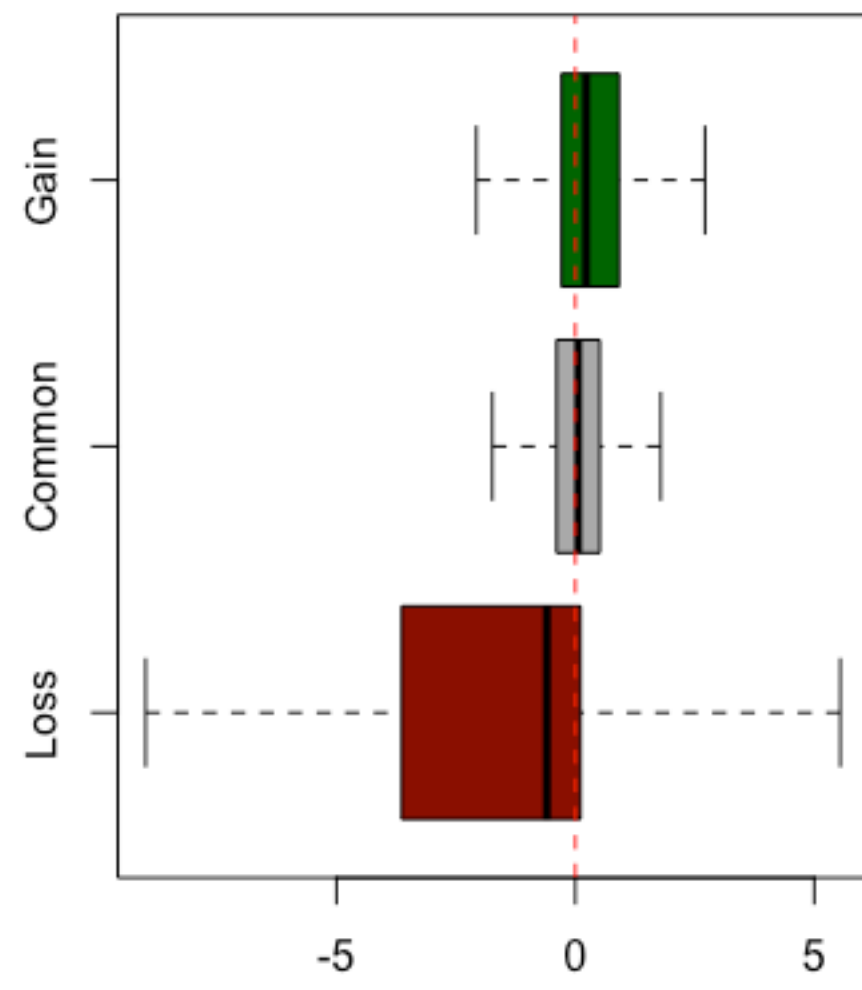
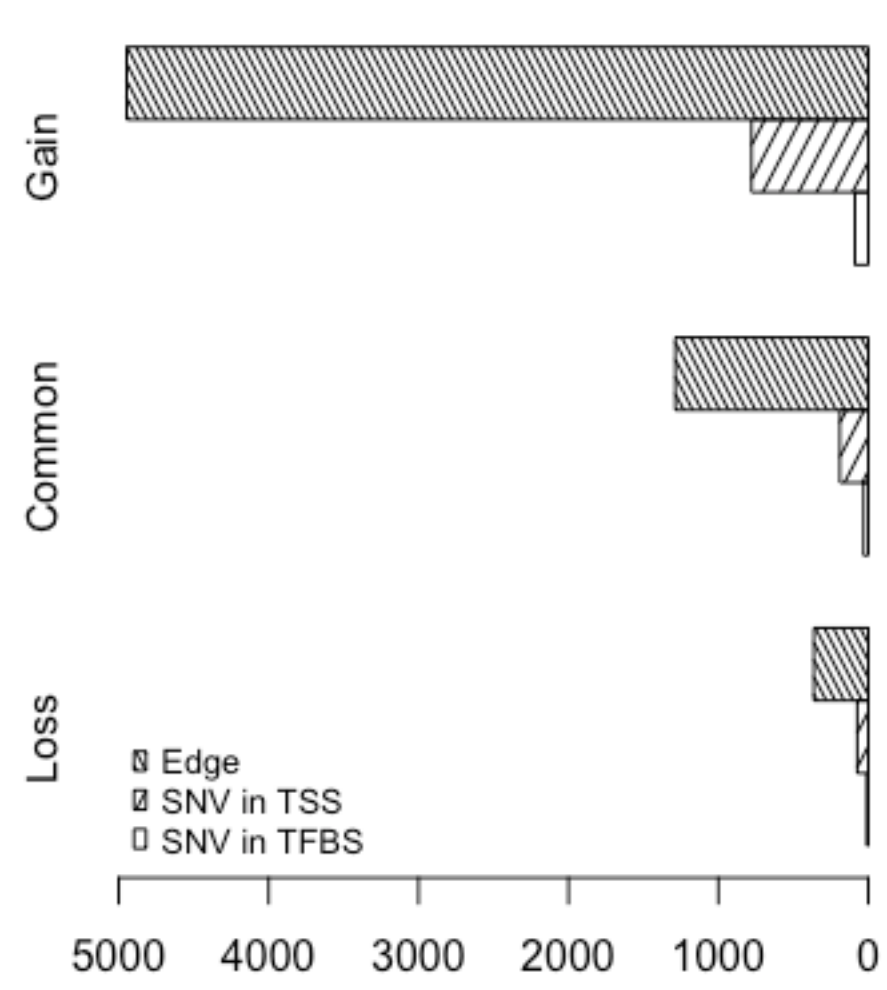


K562-GM12878 Network



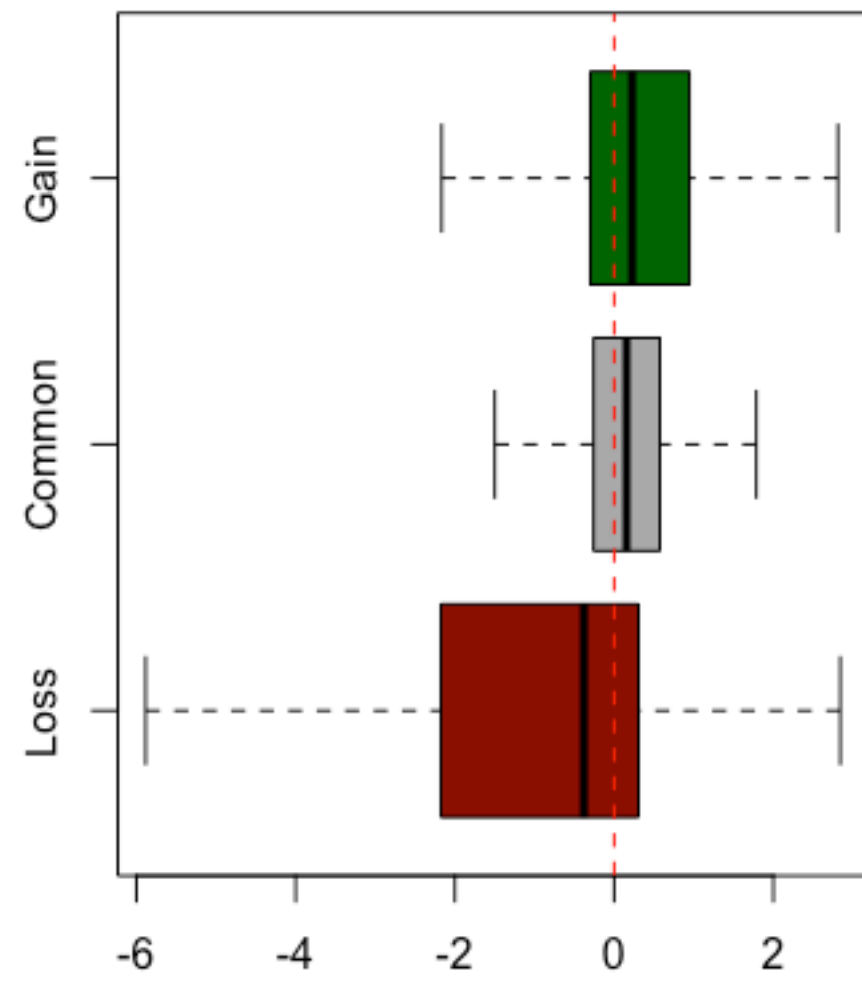
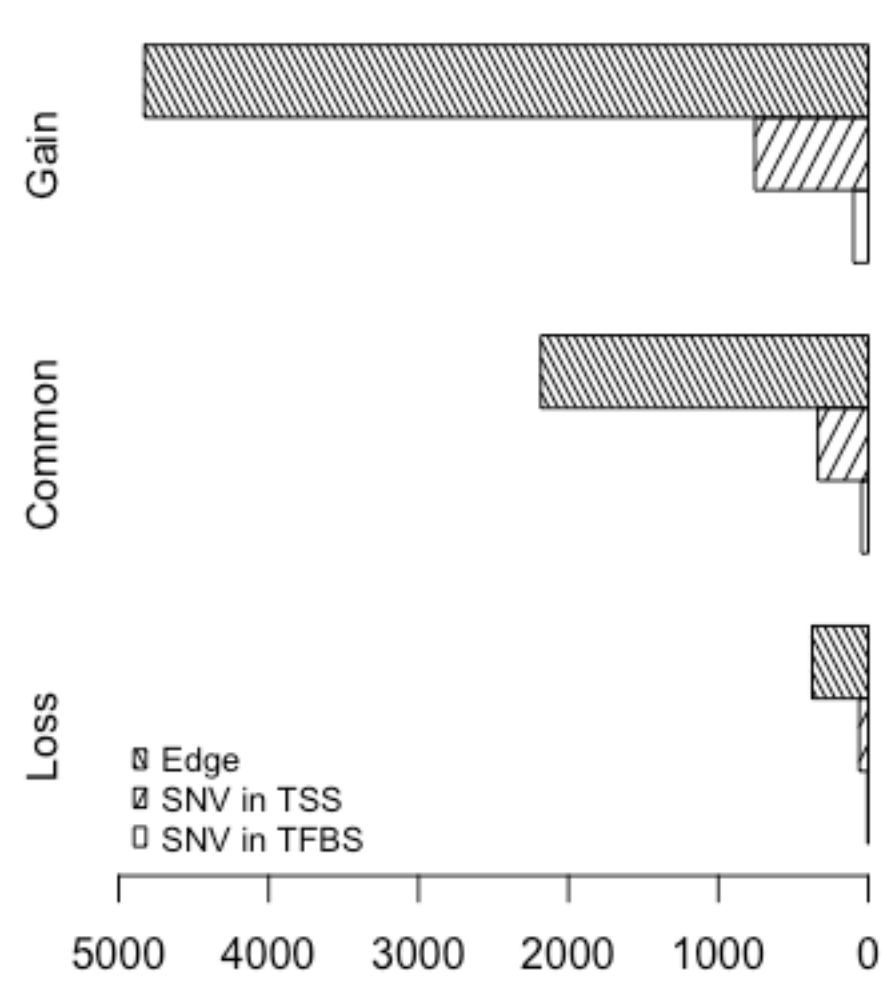
■ rScore_TF2GENE
■ rScore_TF2TF
■ Cooperativity

JUND



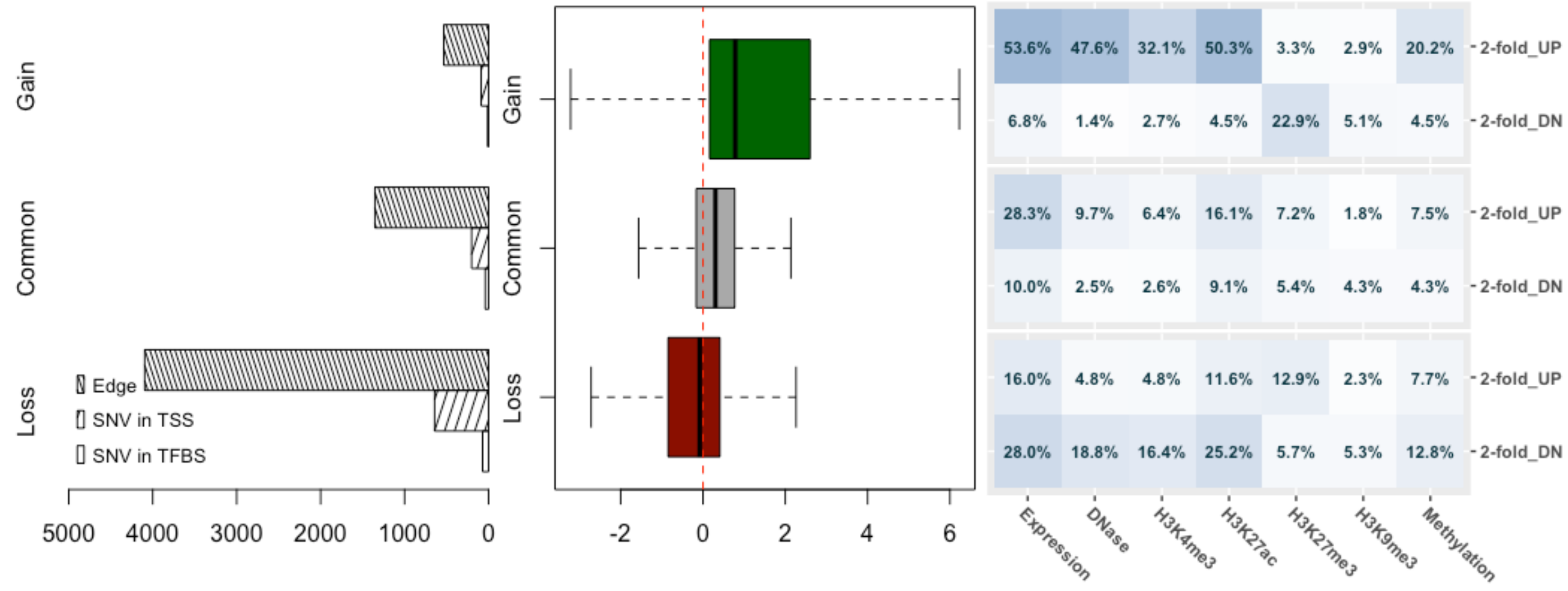
31.1%	24.8%	16.7%	29.7%	7.8%	3.2%	9.9%	-2-fold_UP
15.7%	2.9%	4.2%	9.1%	12.1%	5.3%	7.9%	-2-fold_DN
18.9%	7.0%	6.3%	13.9%	8.3%	0.8%	3.6%	-2-fold_UP
16.7%	6.2%	4.3%	12.4%	5.1%	4.3%	9.8%	-2-fold_DN
11.8%	2.5%	2.8%	5.8%	22.6%	2.2%	8.0%	-2-fold_UP
47.1%	54.8%	49.0%	57.3%	7.4%	10.5%	11.6%	-2-fold_DN
Expression	DNase	H3K4me3	H3K27ac	H3K27me3	H3K9me3	Methylation	

MYC



31.8%	21.6%	16.2%	28.5%	6.4%	2.2%	8.7%	-2-fold_UP
15.7%	4.2%	3.7%	10.7%	13.9%	5.9%	8.4%	-2-fold_DN
19.8%	4.9%	4.4%	12.1%	8.8%	1.5%	4.0%	-2-fold_UP
11.7%	4.1%	2.2%	8.2%	3.8%	4.1%	10.1%	-2-fold_DN
13.2%	6.2%	3.5%	9.7%	20.0%	5.1%	14.3%	-2-fold_UP
40.8%	34.6%	34.3%	43.5%	4.1%	7.0%	10.8%	-2-fold_DN
Expression	DNase	H3K4me3	H3K27ac	H3K27me3	H3K9me3	Methylation	

HDGF



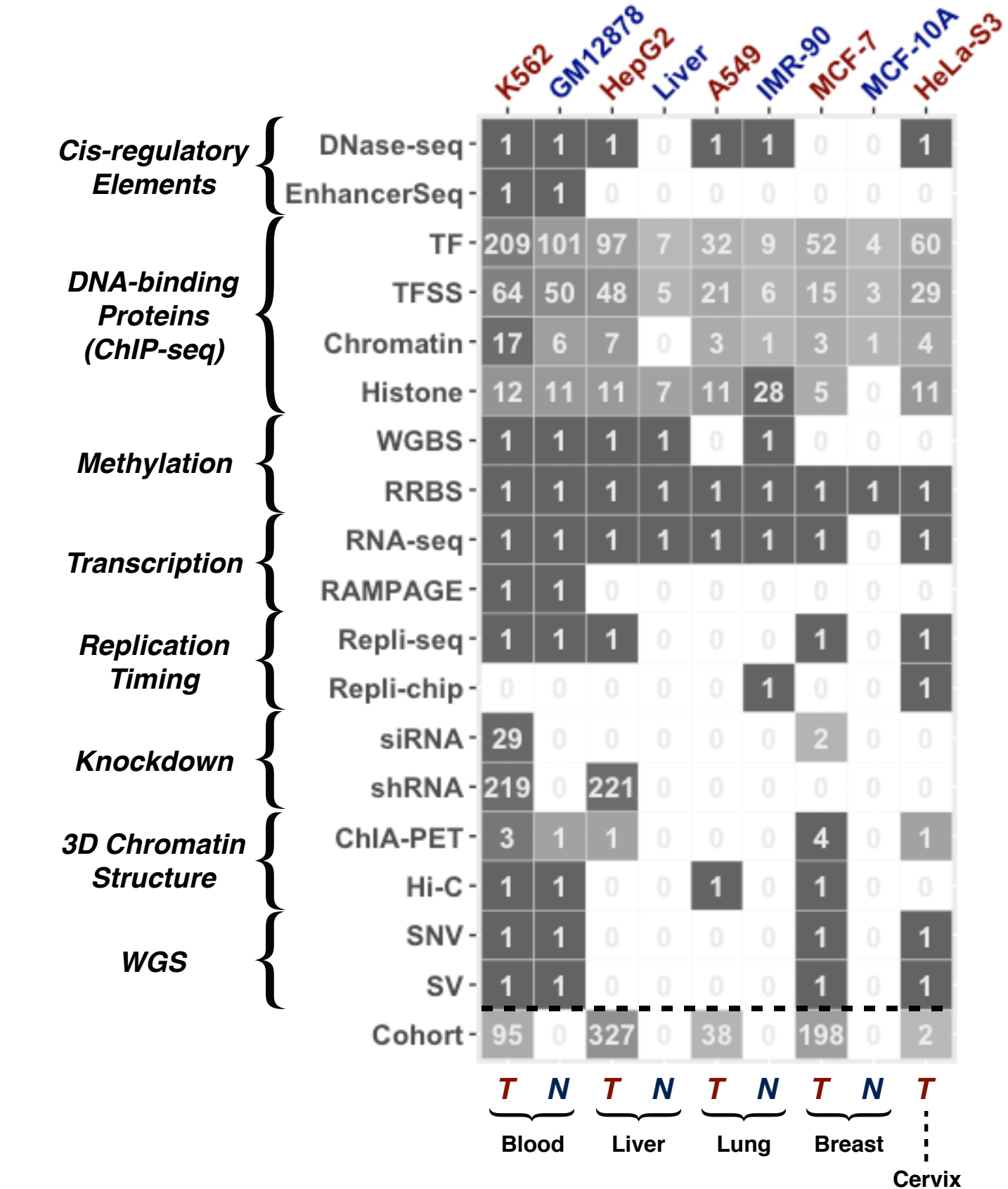
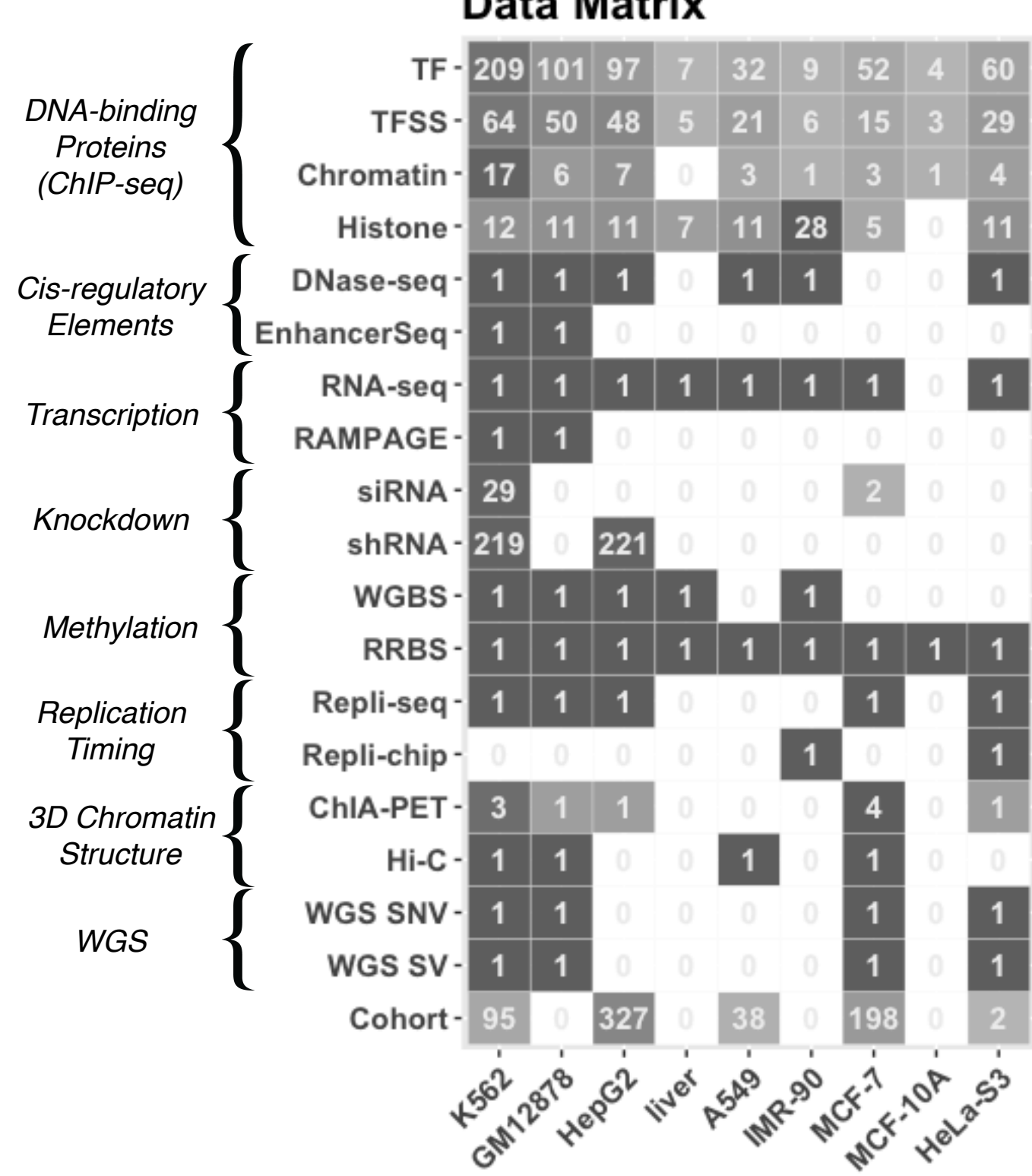
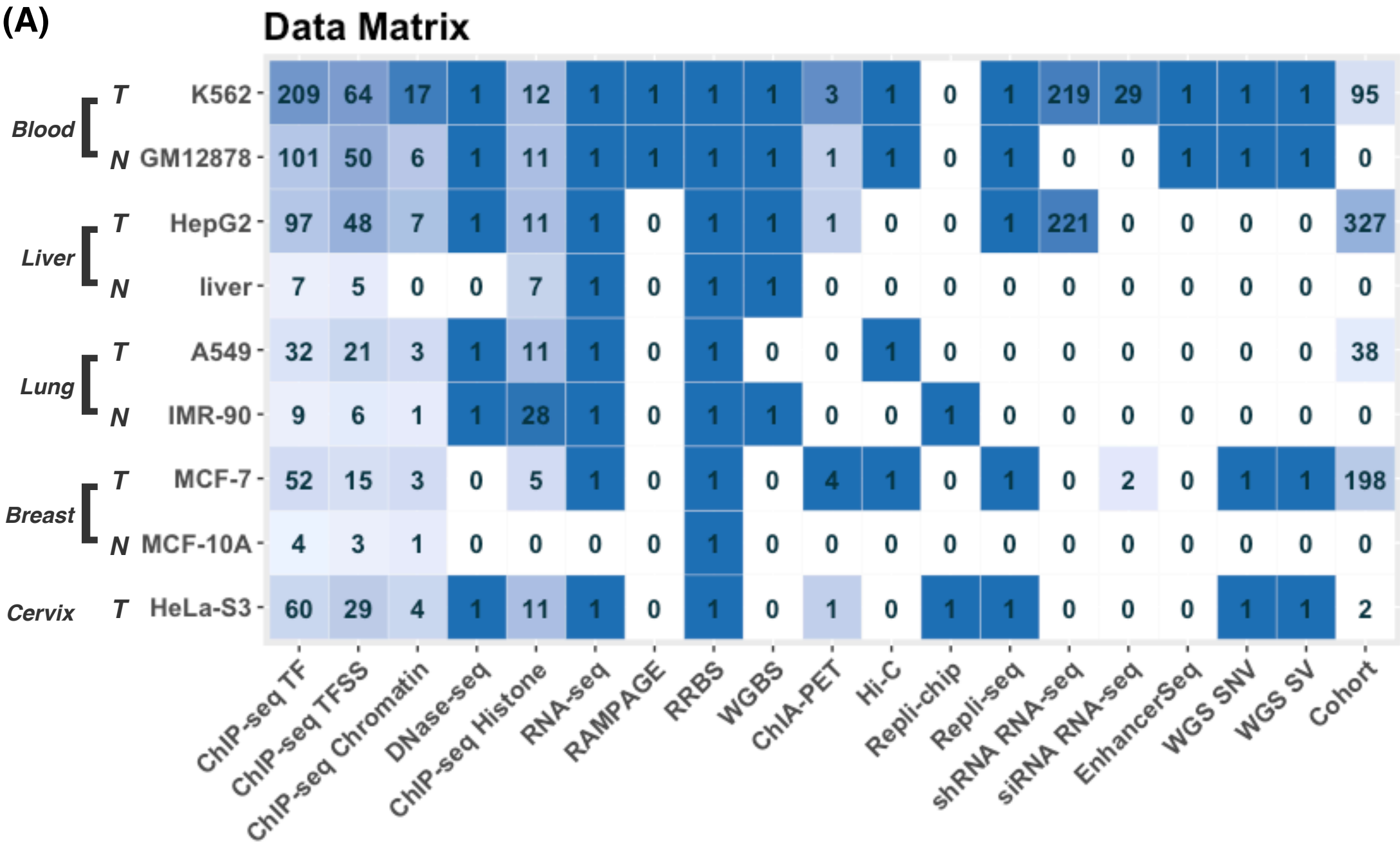


Figure 1

A

Data Matrix

		ChIP-seq TF	ChIP-seq TFSS	ChIP-seq Chromatin	DNase-seq	Histone	RNA-seq	RAMPAGE	RRBS	WGBS	ChIA-PET	Hi-C	Repli-chip	Repli-seq	shRNA	RNA-seq	siRNA	RNA-seq	EnhancerSeq	WGS SNV	WGS SV	Cohort
Blood	T K562	209	64	17	1	12	1	1	1	1	3	1	0	1	219	29	1	1	1	1	1	95
	N GM12878	101	50	6	1	11	1	1	1	1	1	1	0	1	0	0	1	1	1	1	1	0
Liver	T HepG2	97	48	7	1	11	1	0	1	1	1	0	0	1	221	0	0	0	0	0	0	327
	N liver	7	5	0	0	7	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Lung	T A549	32	21	3	1	11	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	38
	N IMR-90	9	6	1	1	28	1	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0
Breast	T MCF-7	52	15	3	0	5	1	0	1	0	4	1	0	1	0	2	0	1	1	1	1	198
	N MCF-10A	4	3	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Cervix	T HeLa-S3	60	29	4	1	11	1	0	1	0	1	0	1	1	0	0	0	0	1	1	1	2

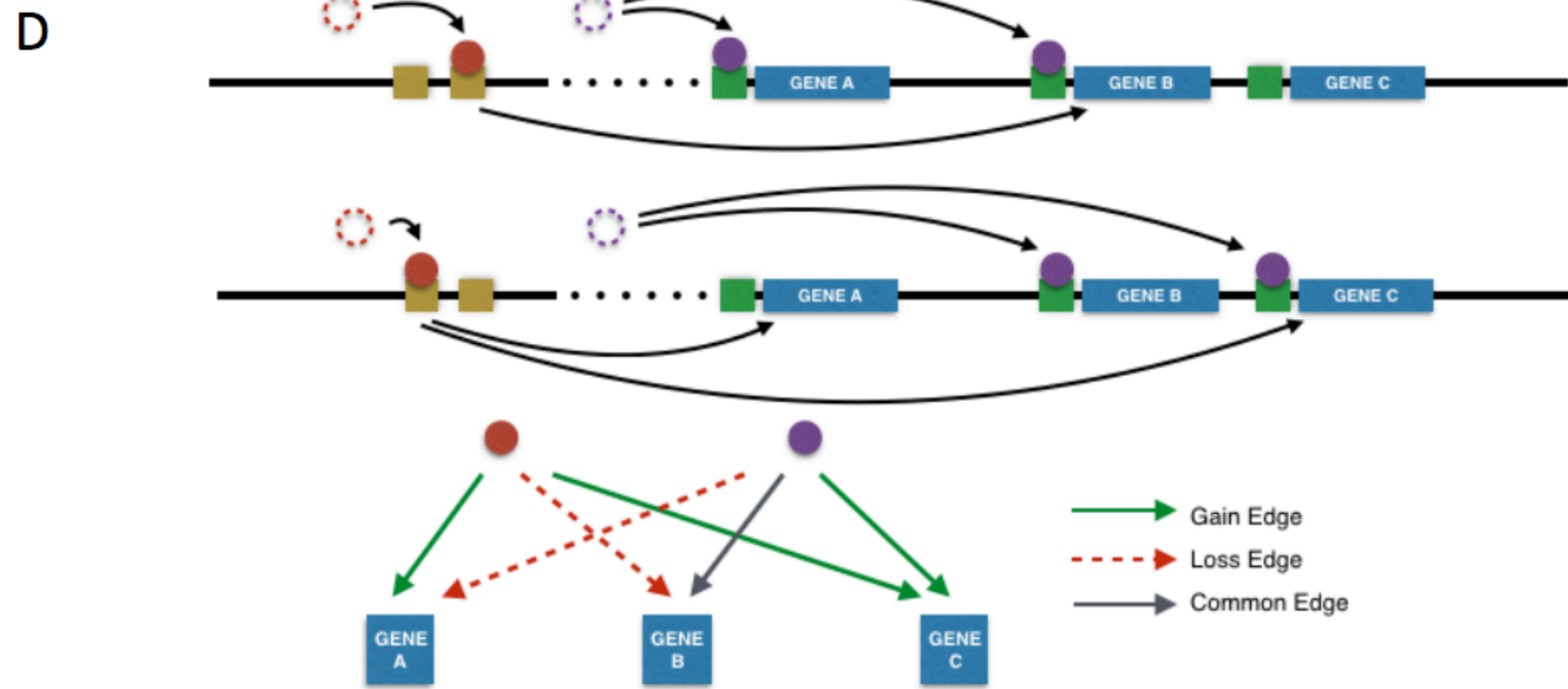
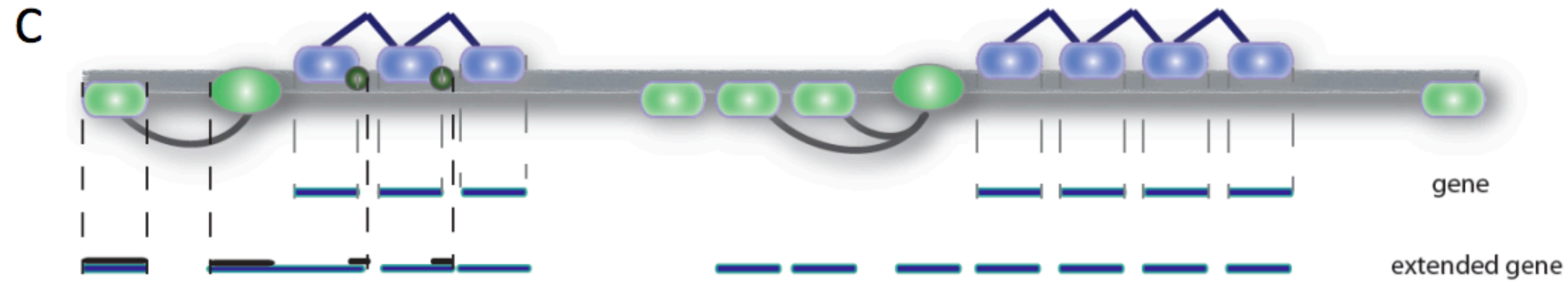
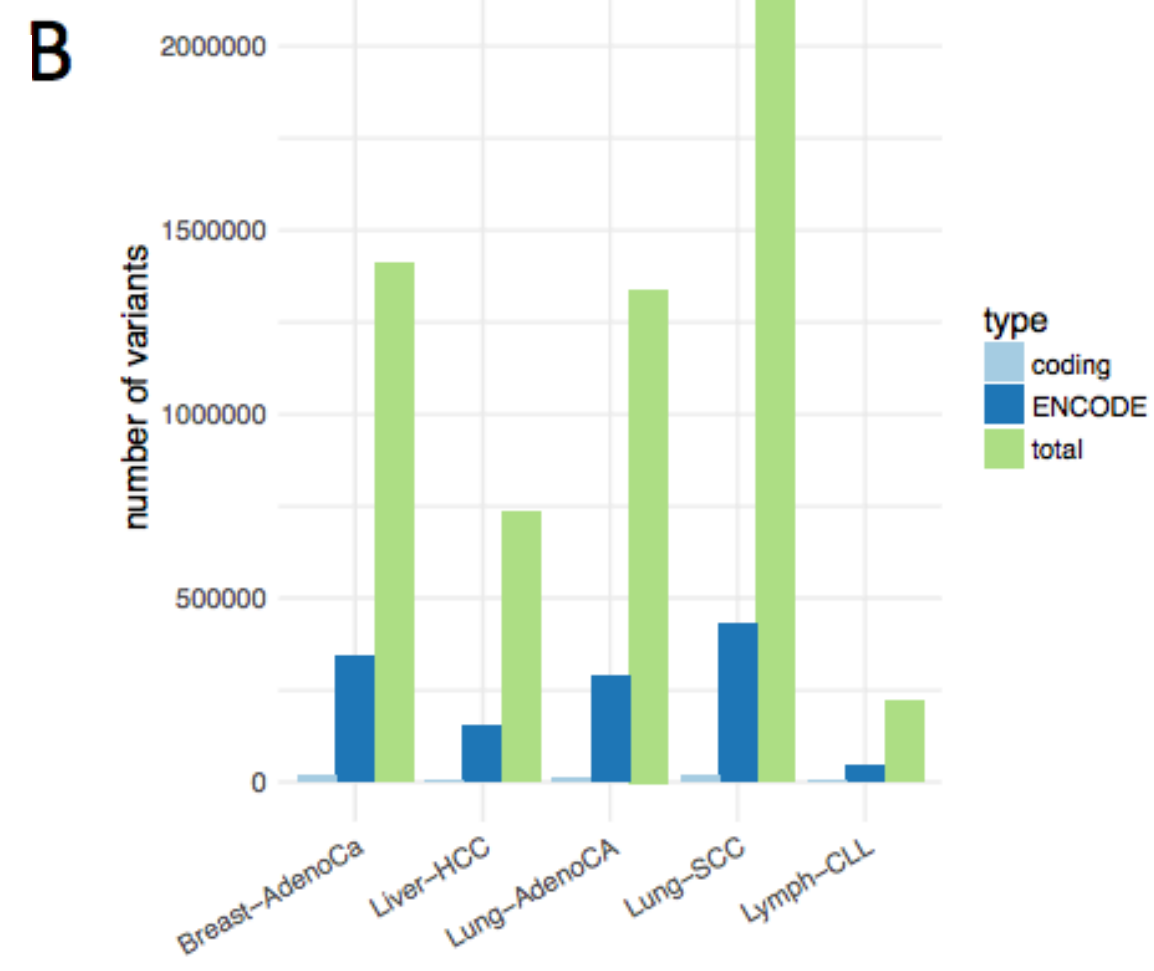


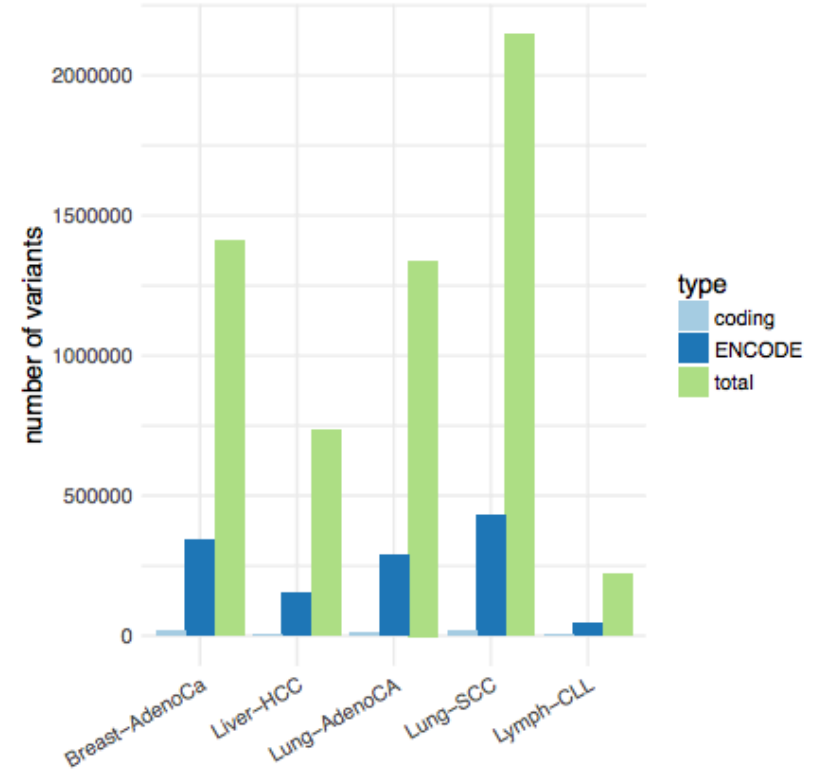
Figure 1

Data Matrix

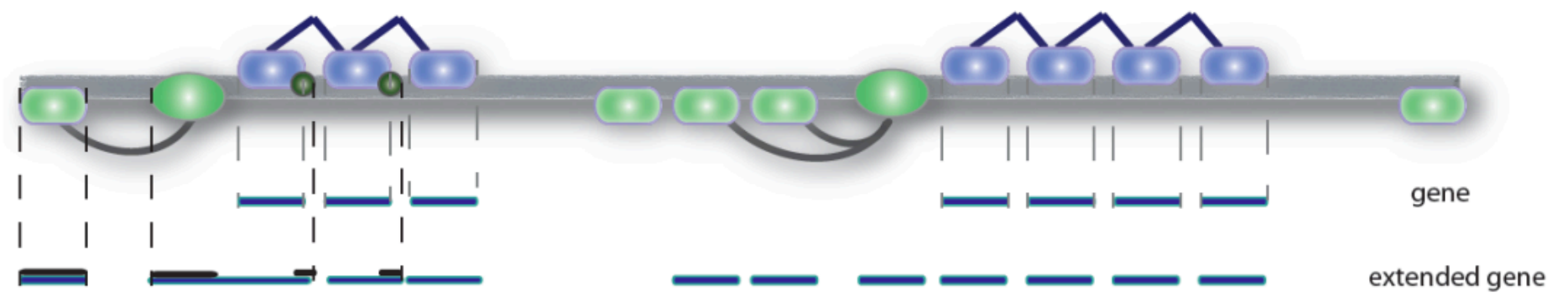
		K562		GM12878		HepG2		Liver		A549		IMR-90		MCF-7		MCF-10A		HeLa-S3		
Cis-regulatory Elements	DNase-seq	1	1	1	0	1	1	0	0	1	1	0	0	1						
	EnhancerSeq	1	1	0	0	0	0	0	0	0	0	0	0	0						
DNA-binding Proteins (ChIP-seq)	TF	209	101	97	7	32	9	52	4	60										
	TFSS	64	50	48	5	21	6	15	3	29										
	Chromatin	17	6	7	0	3	1	3	1	4										
Methylation	Histone	12	11	11	7	11	28	5	0	11										
	WGBS	1	1	1	1	0	1	0	0	0										
	RRBS	1	1	1	1	1	1	1	1	1										
Transcription	RNA-seq	1	1	1	1	1	1	1	1	0	1									
	RAMPAGE	1	1	0	0	0	0	0	0	0										
Replication Timing	Repli-seq	1	1	1	0	0	0	1	0	1										
	Repli-chip	0	0	0	0	0	1	0	0	1										
Knockdown	siRNA	29	0	0	0	0	0	2	0	0										
	shRNA	219	0	221	0	0	0	0	0	0										
3D Chromatin Structure	ChIA-PET	3	1	1	0	0	0	4	0	1										
	Hi-C	1	1	0	0	1	0	1	0	0										
	SNV	1	1	0	0	0	0	1	0	1										
WGS	SV	1	1	0	0	0	0	1	0	1										
	Cohort	95	0	327	0	38	0	198	0	2										

T N T N T N T N T
 Blood Liver Lung Breast Cervix

B



C



D

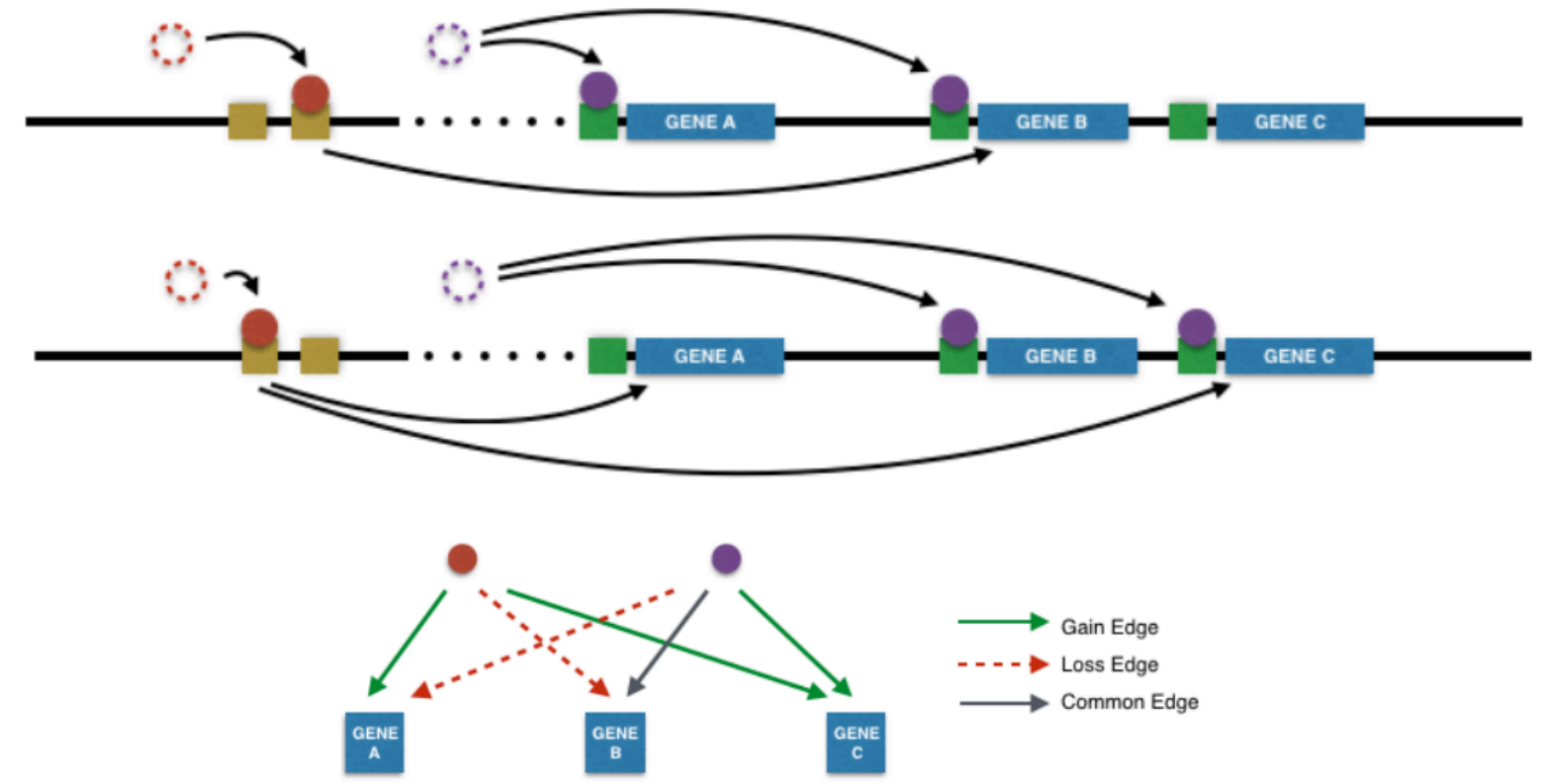


Figure 1

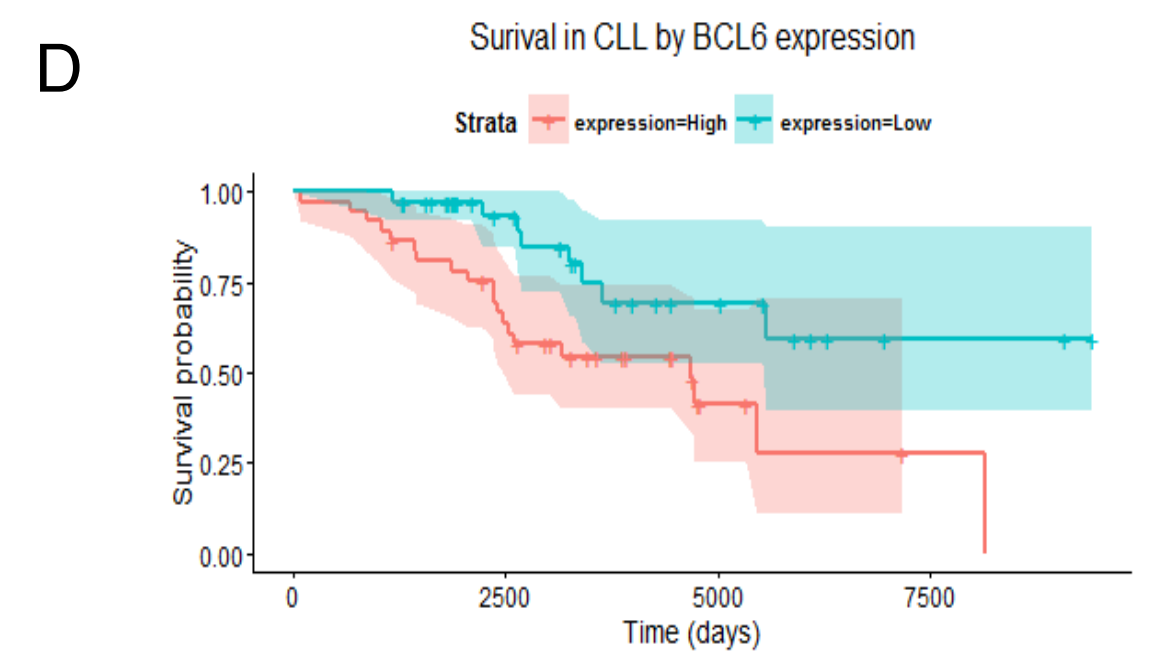
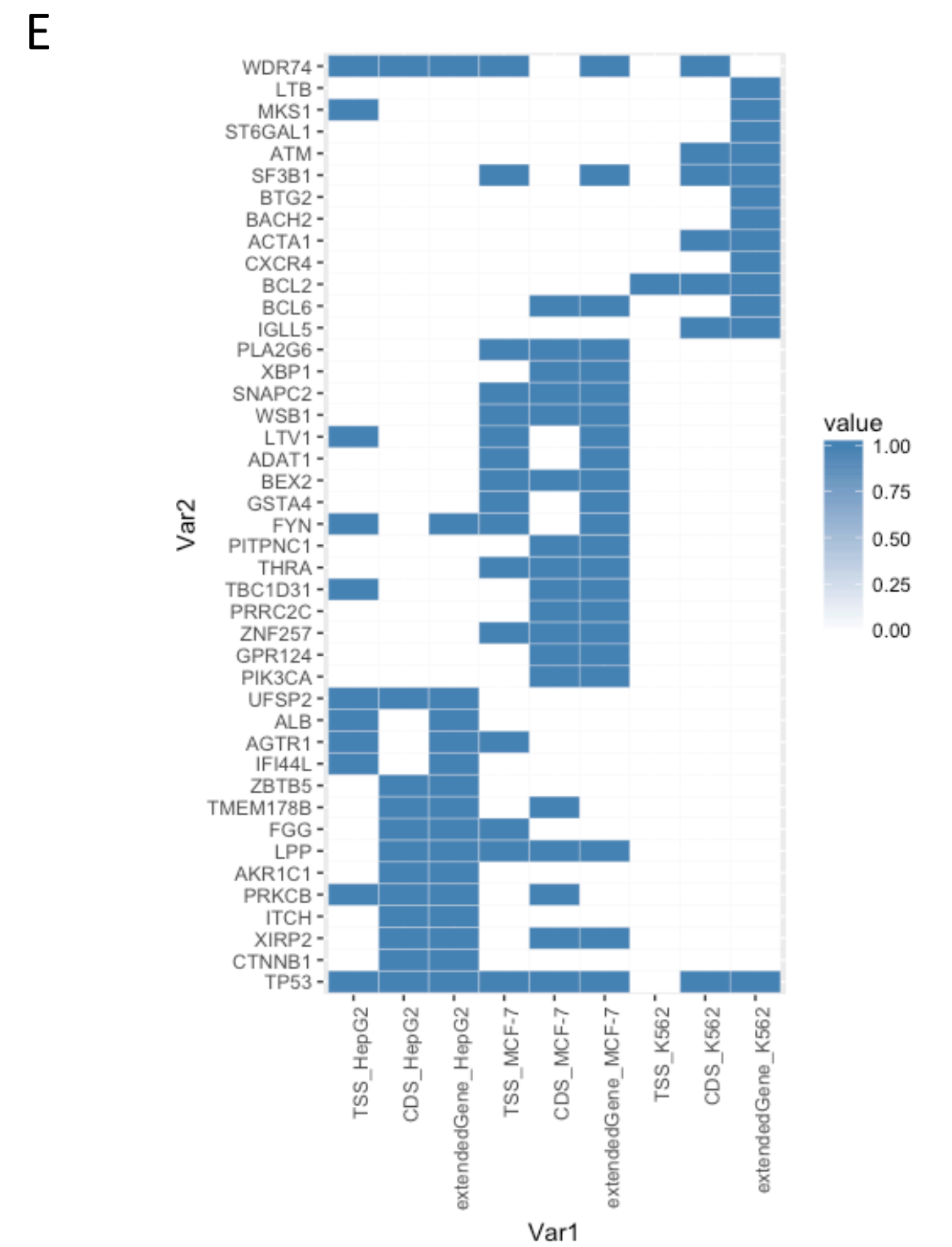
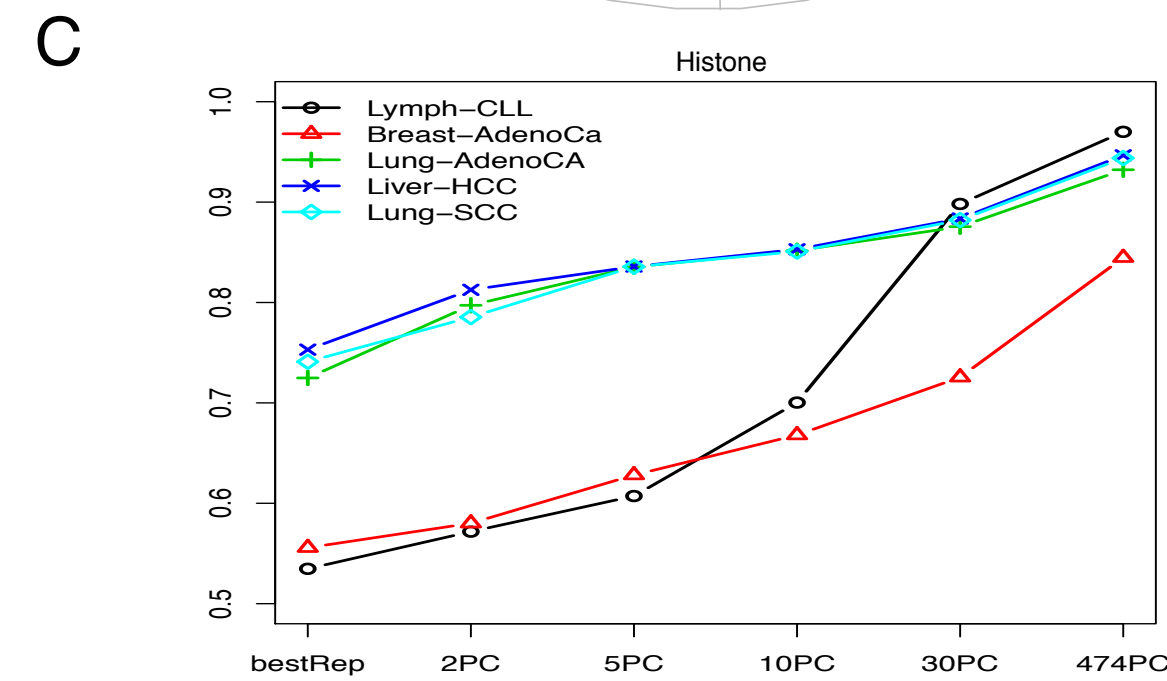
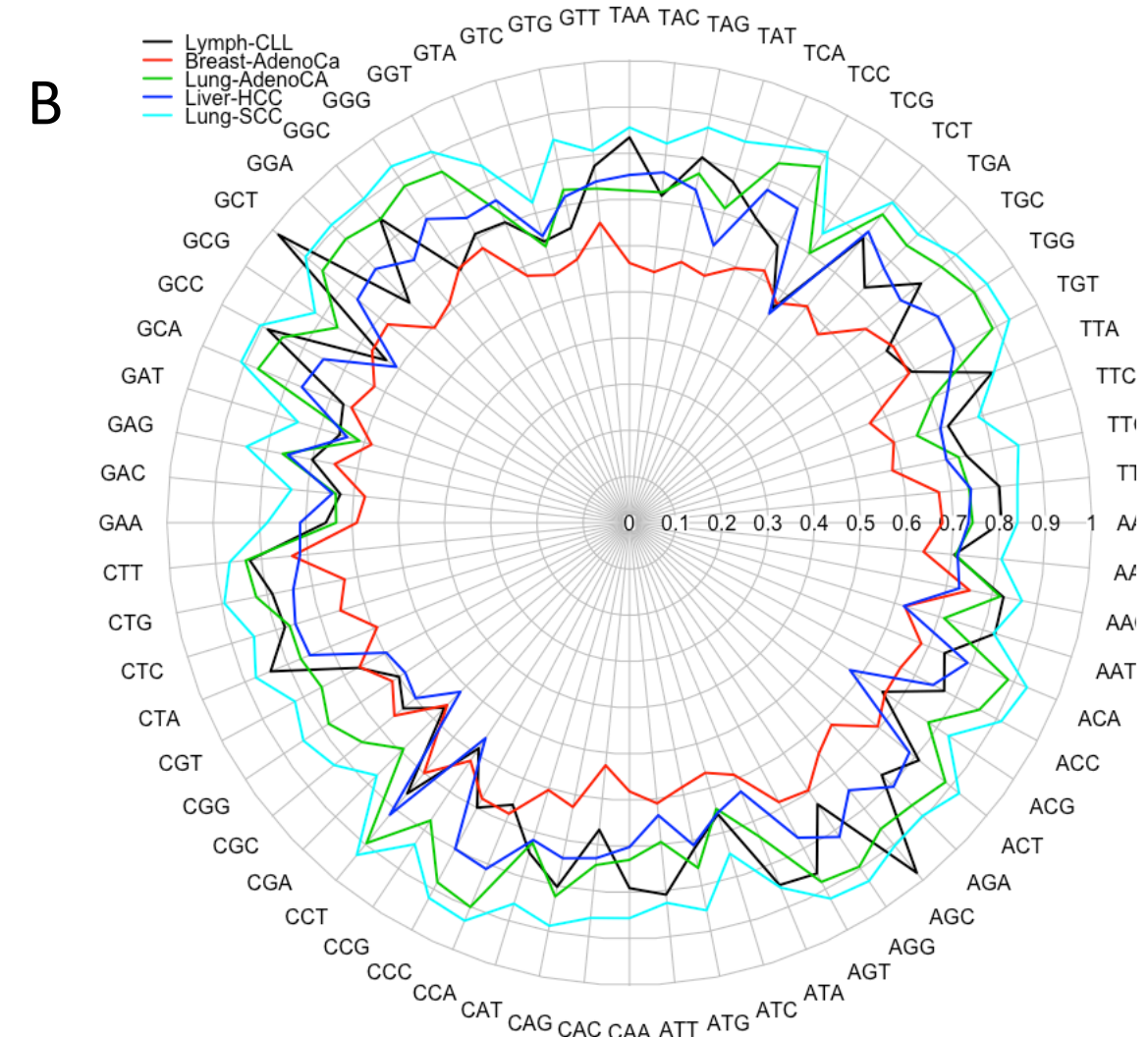
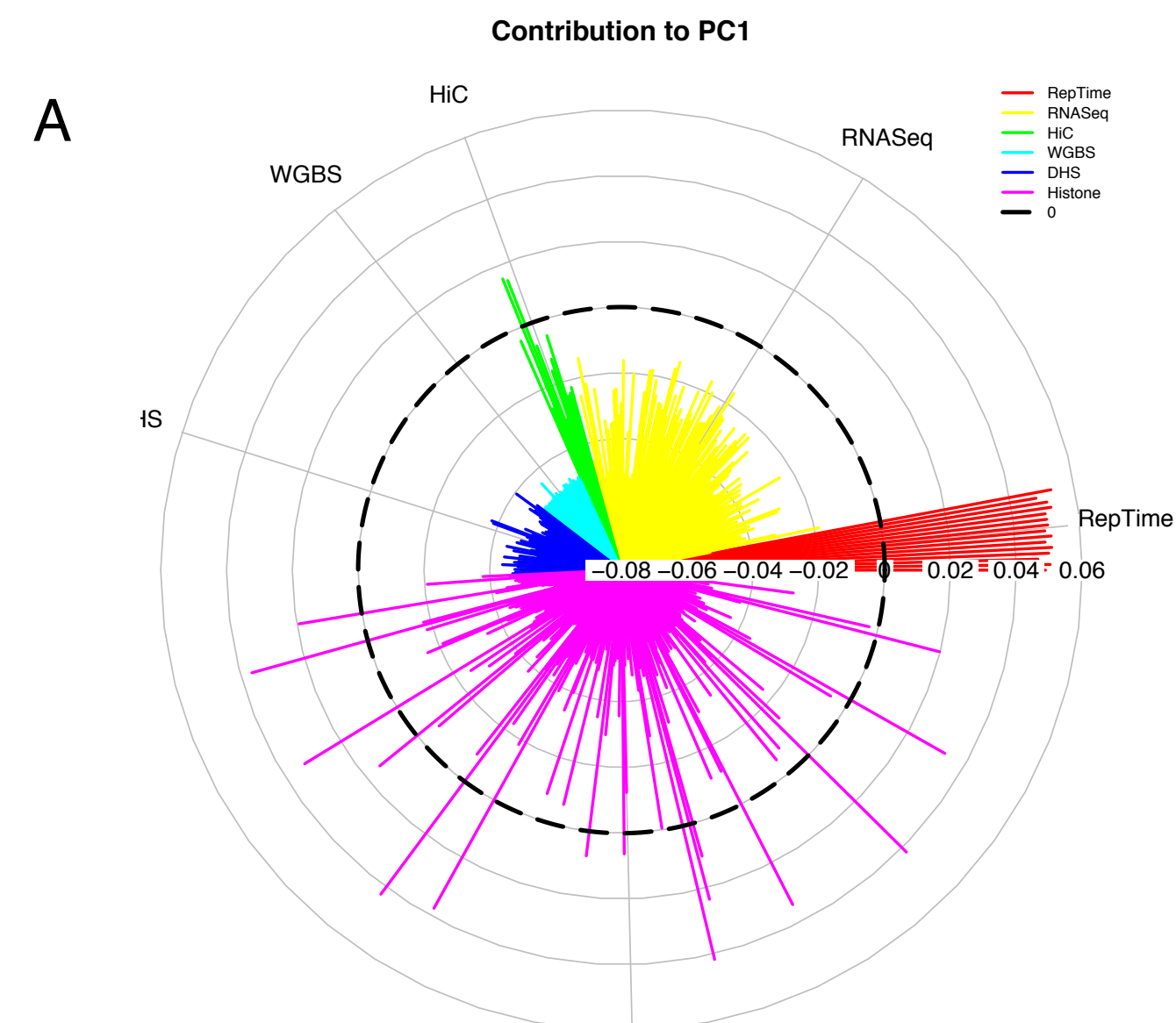
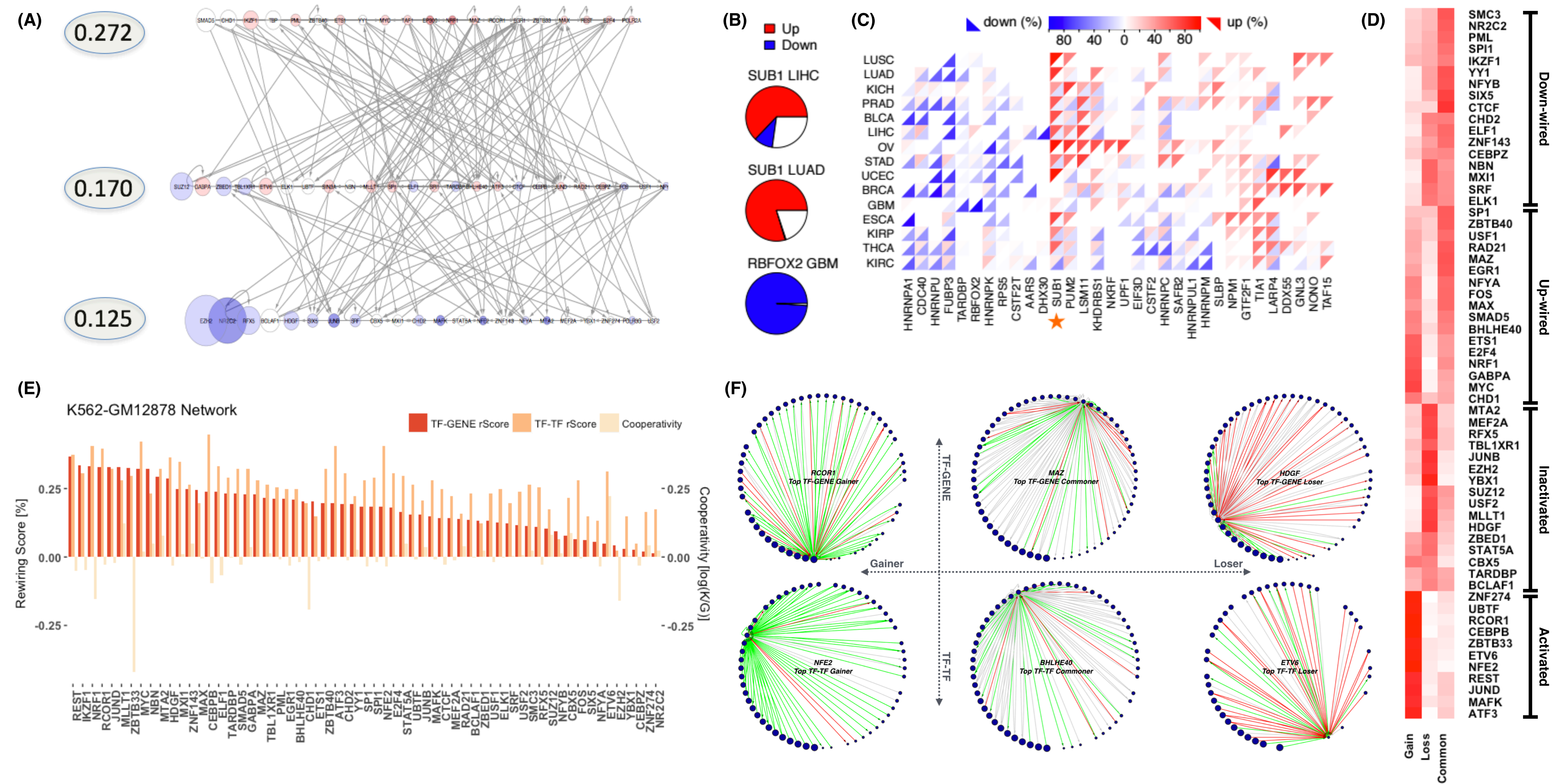


Figure 2



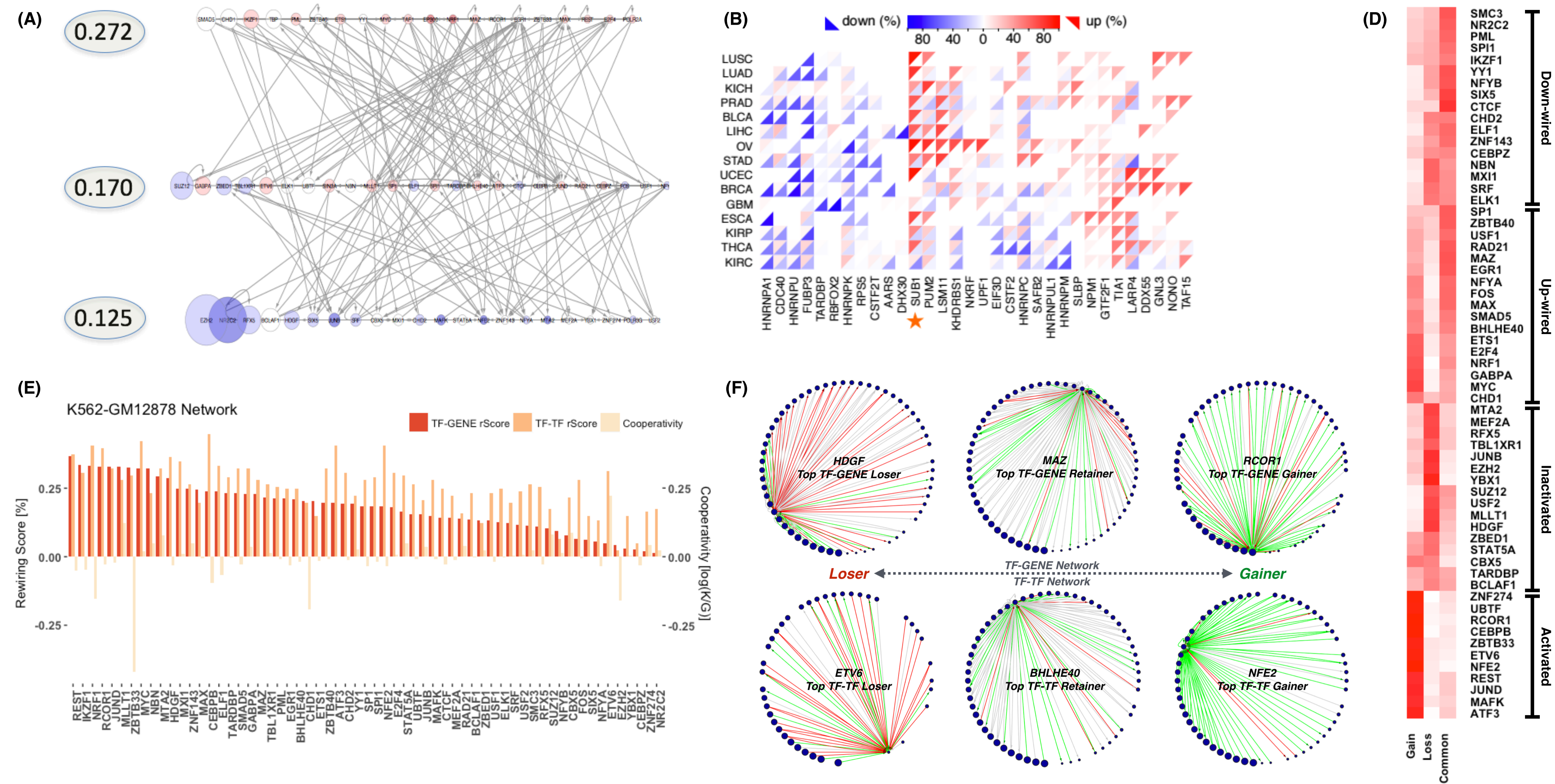


Figure 3

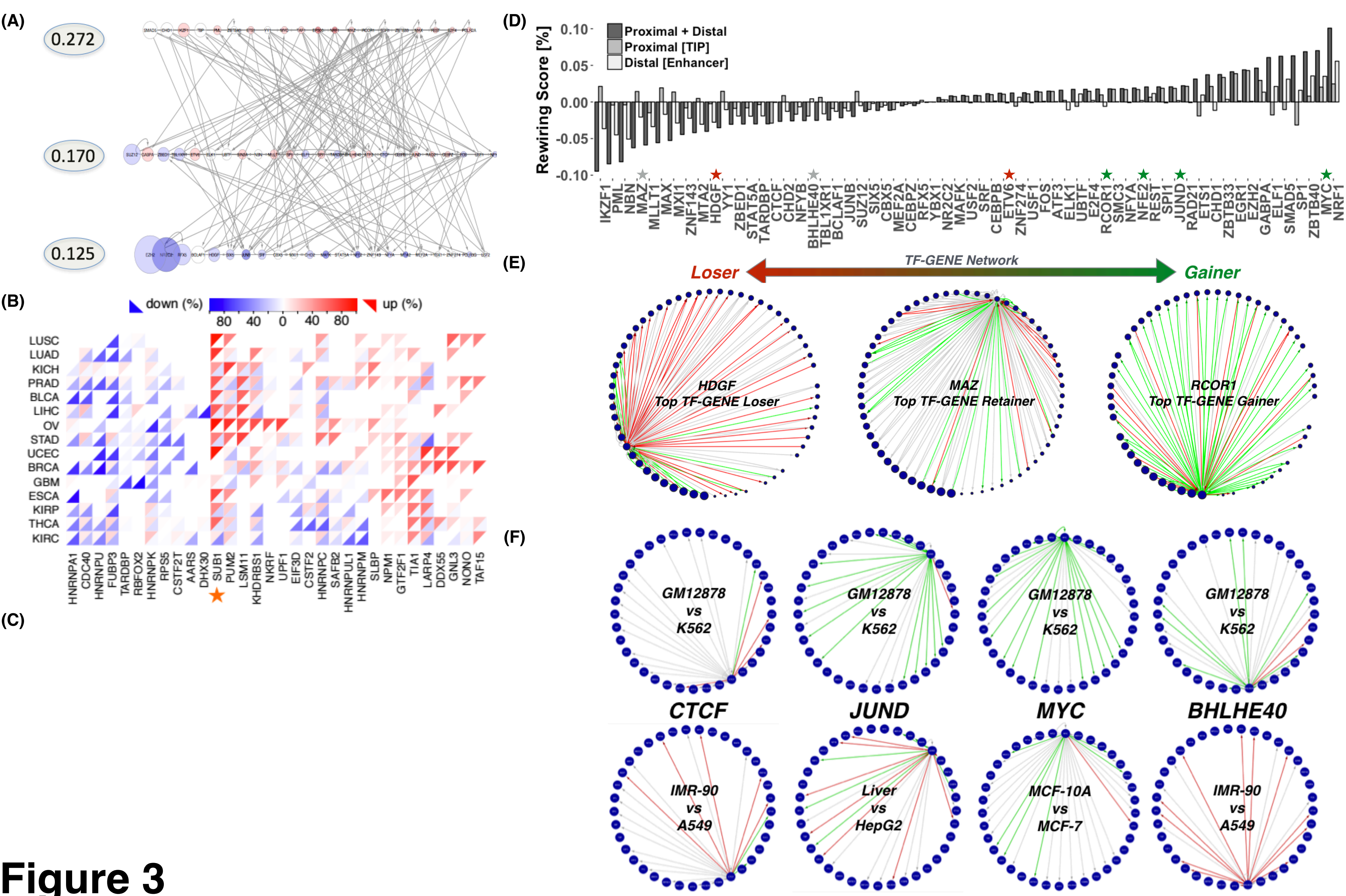


Figure 3

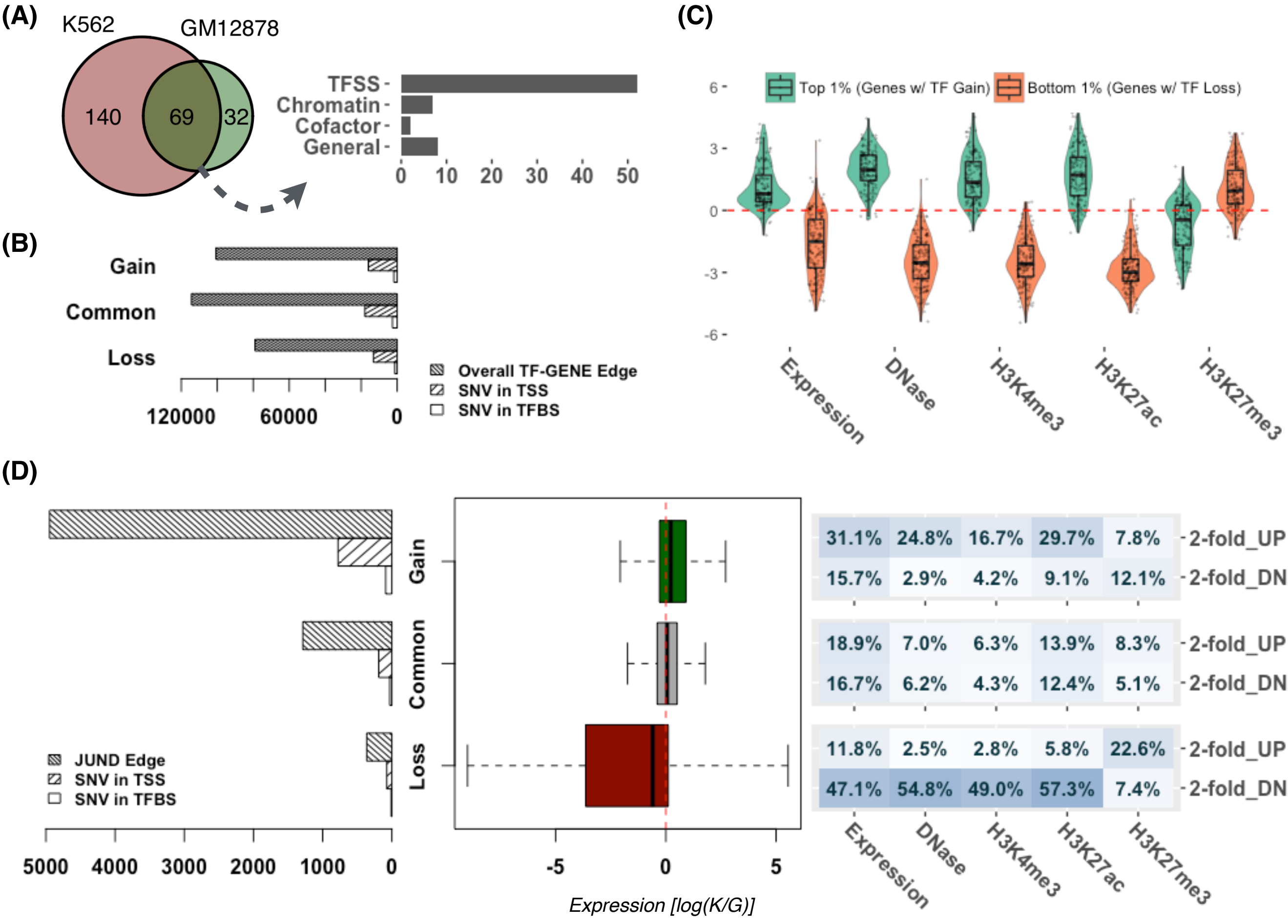
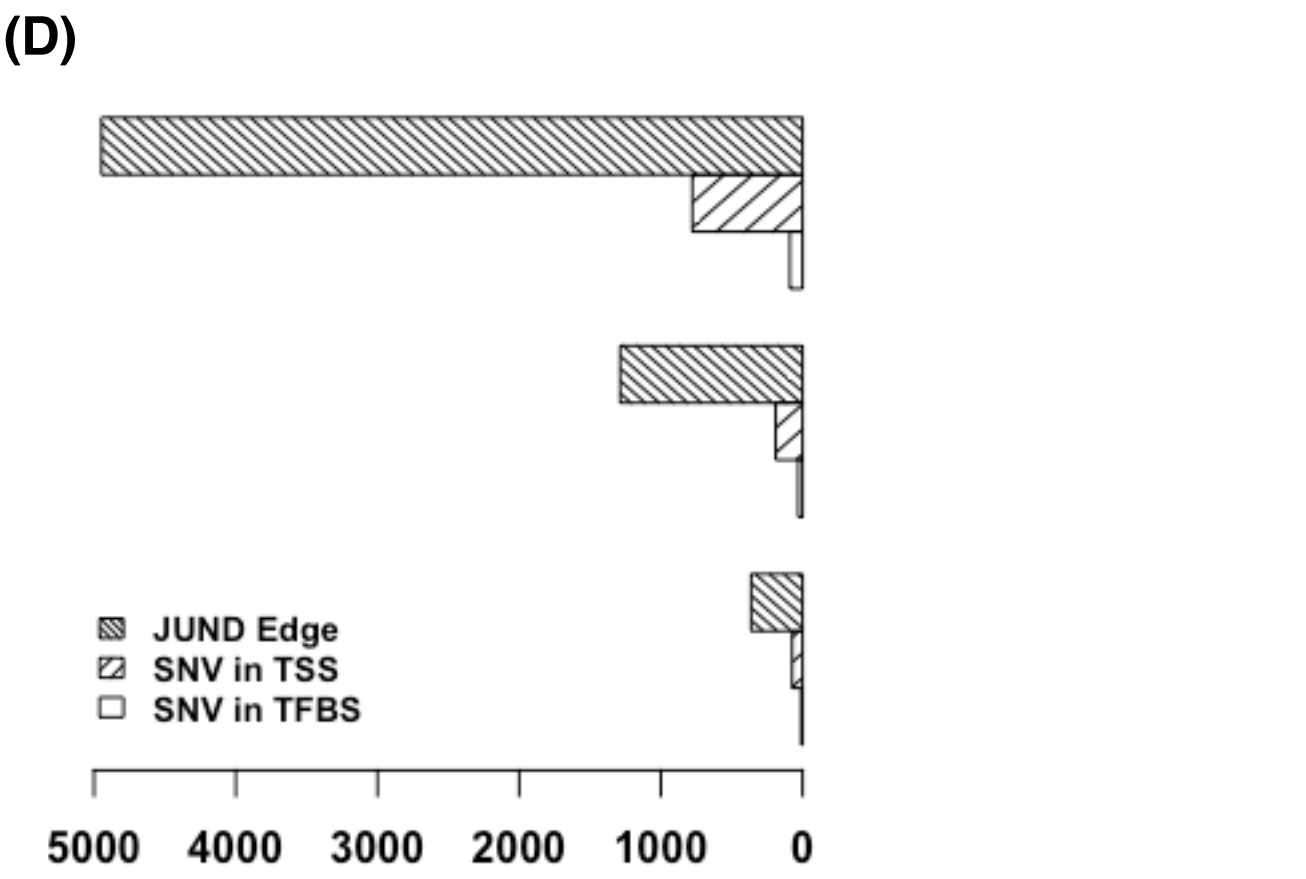
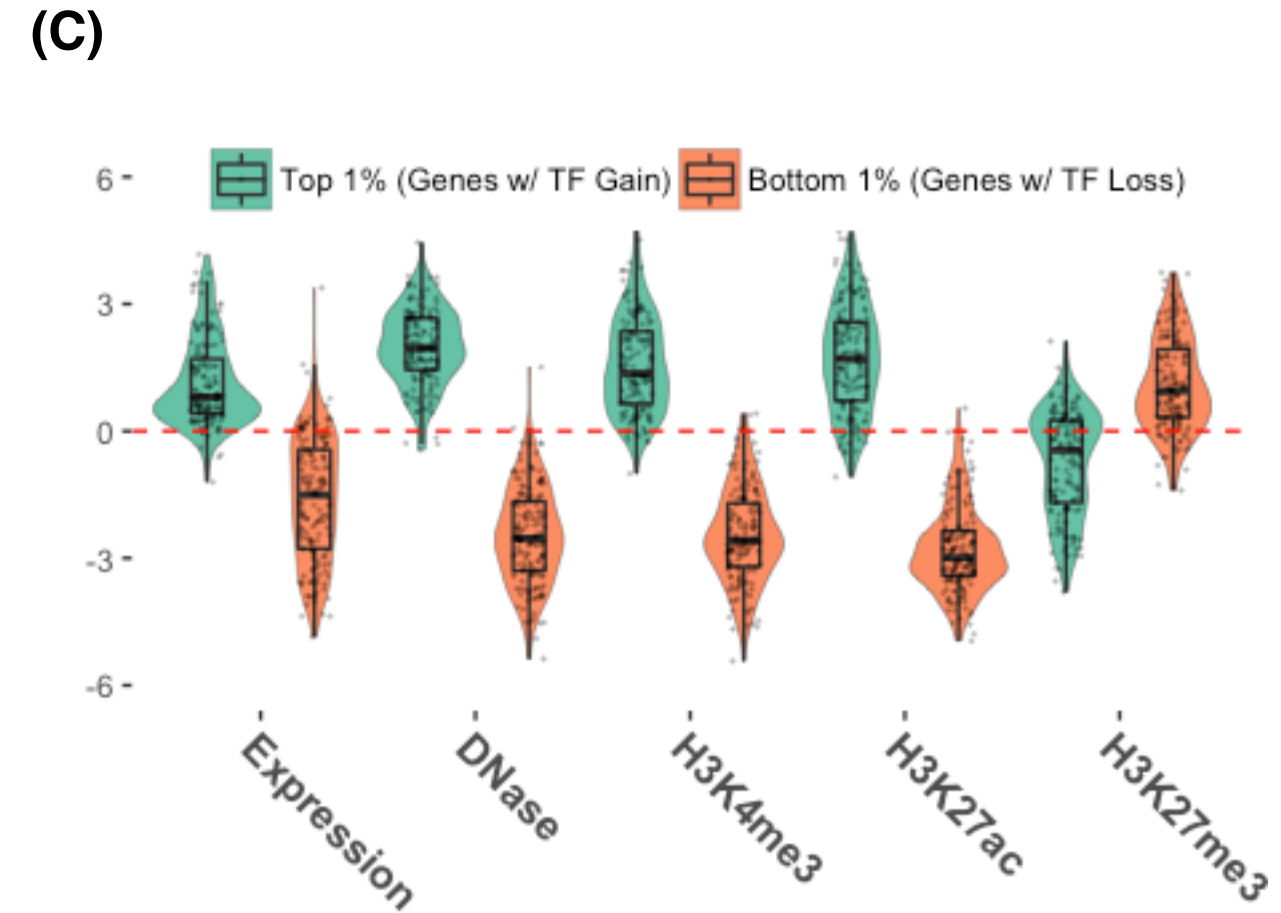
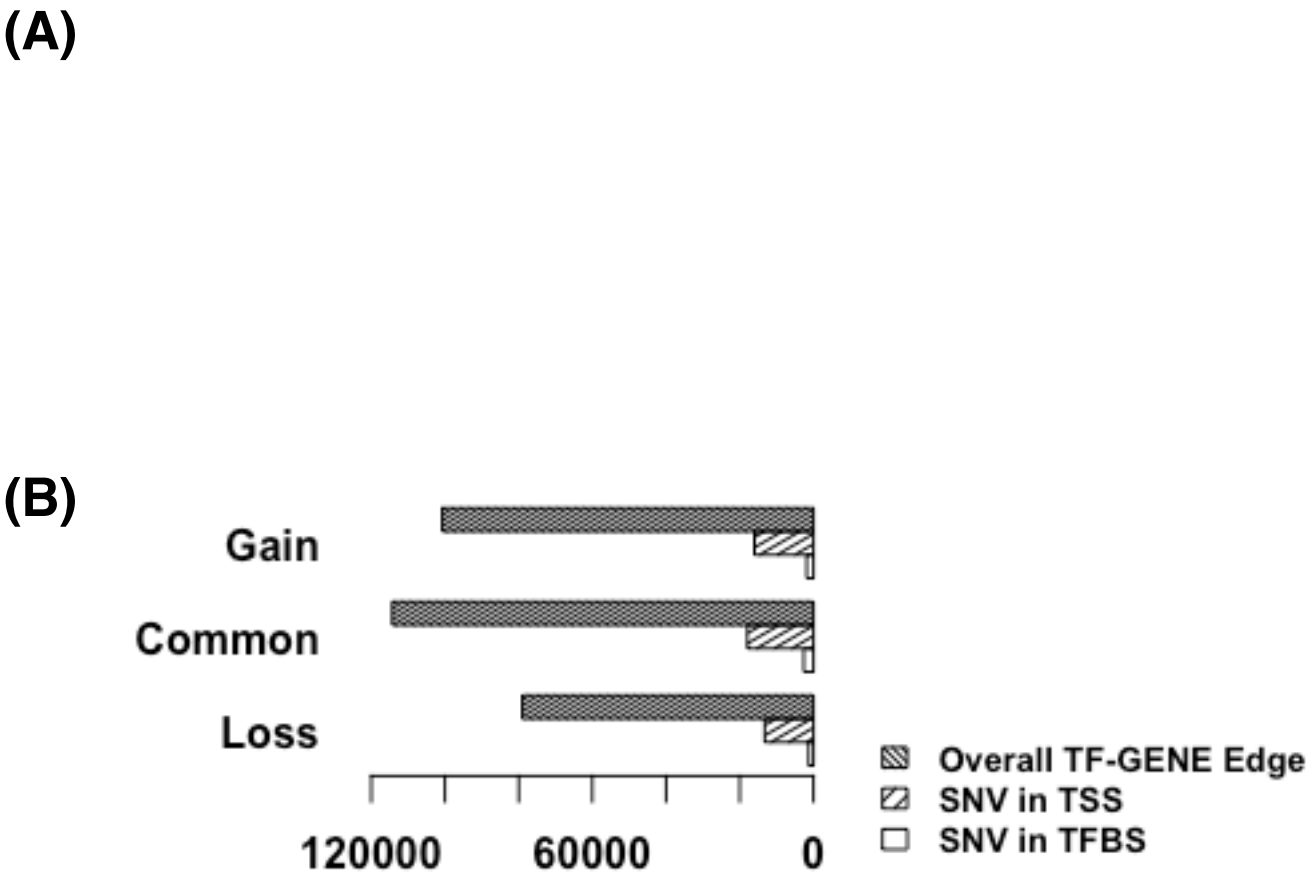


Figure 4



31.1%	24.8%	16.7%	29.7%	7.8%	-2-fold_UP
15.7%	2.9%	4.2%	9.1%	12.1%	-2-fold_DN
18.9%	7.0%	6.3%	13.9%	8.3%	-2-fold_UP
16.7%	6.2%	4.3%	12.4%	5.1%	-2-fold_DN
11.8%	2.5%	2.8%	5.8%	22.6%	-2-fold_UP
47.1%	54.8%	49.0%	57.3%	7.4%	-2-fold_DN
Expression	DNase	H3K4me3	H3K27ac	H3K27me3	

Figure 4

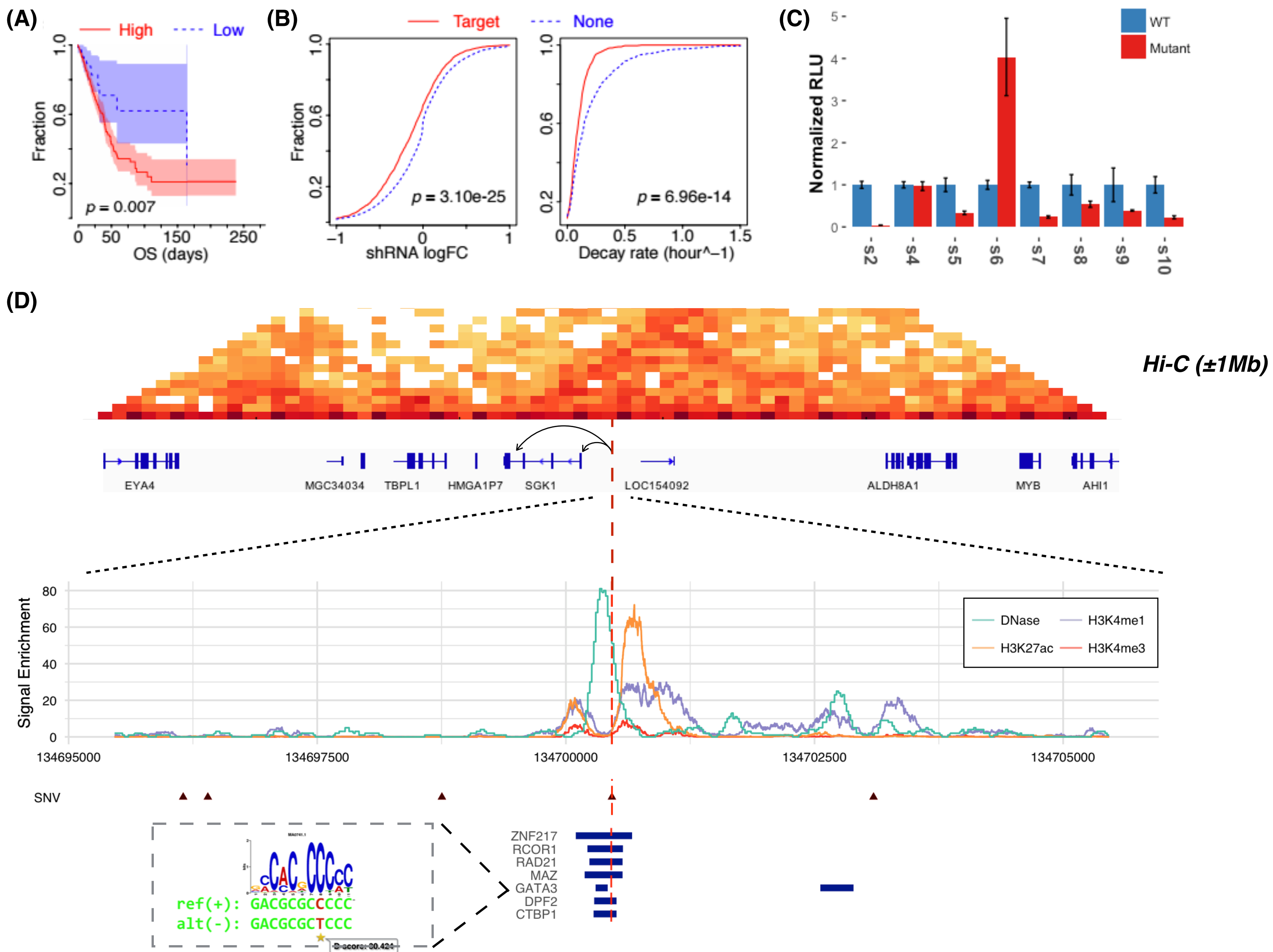


Figure 5

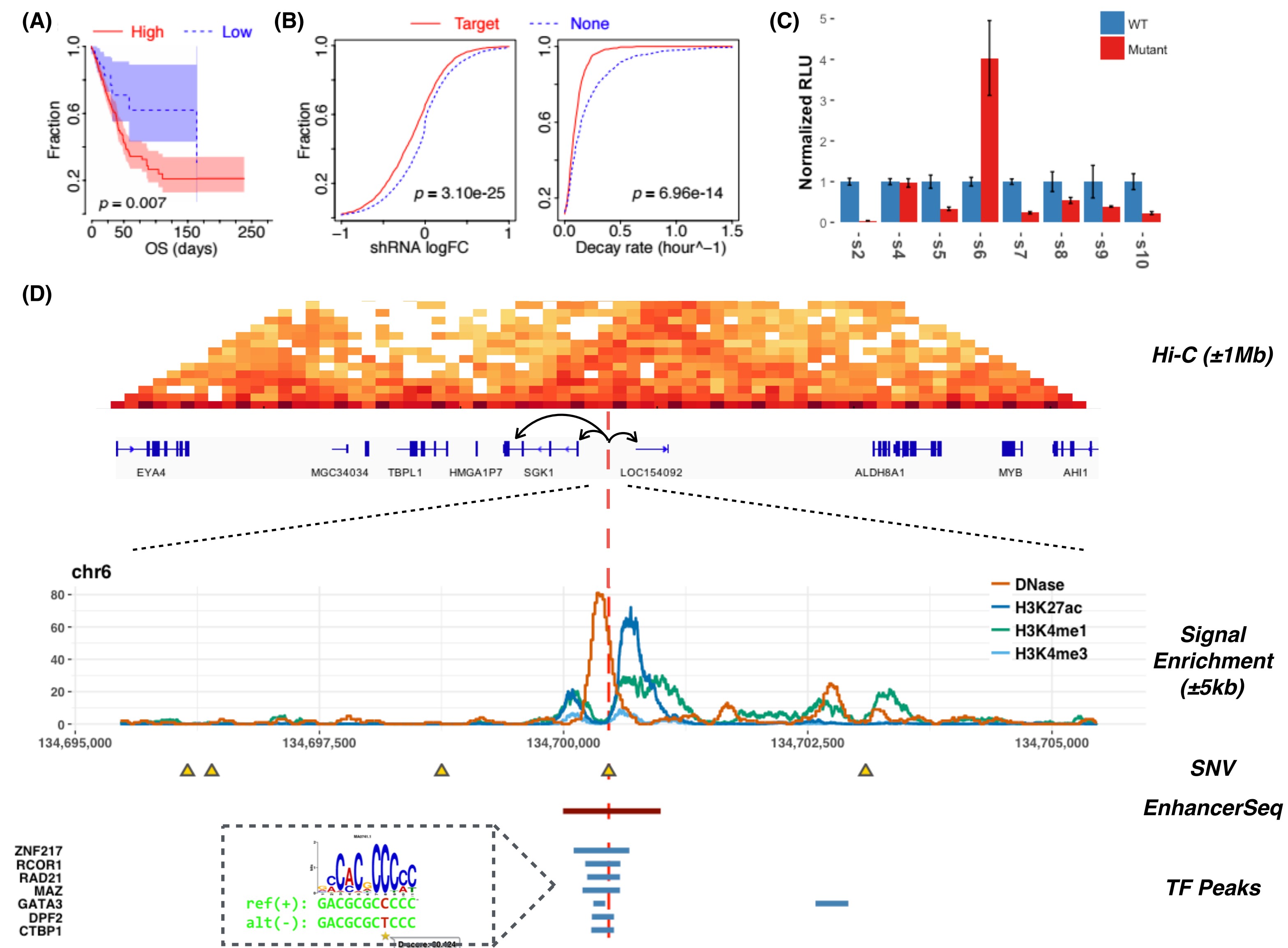


Figure 5

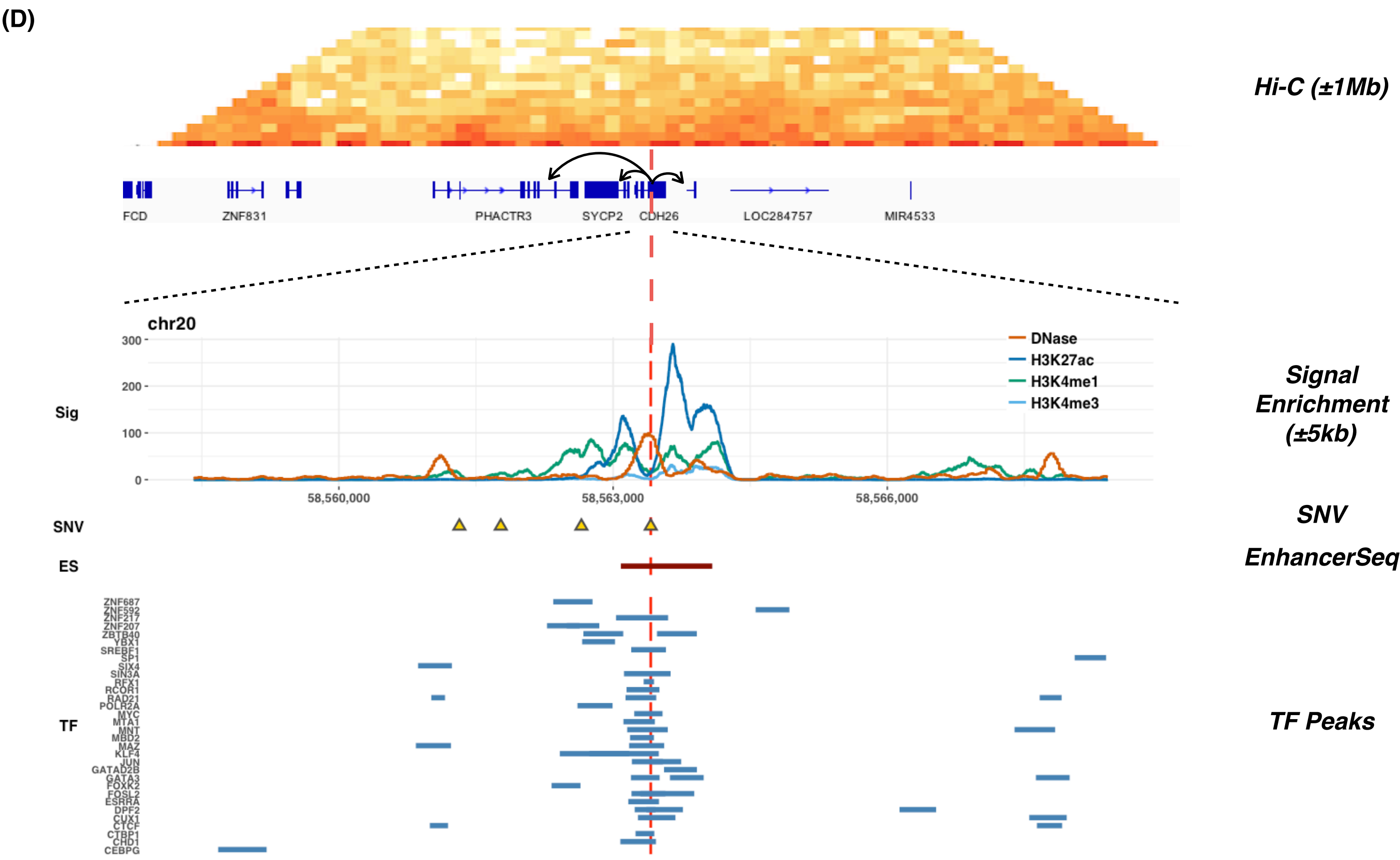
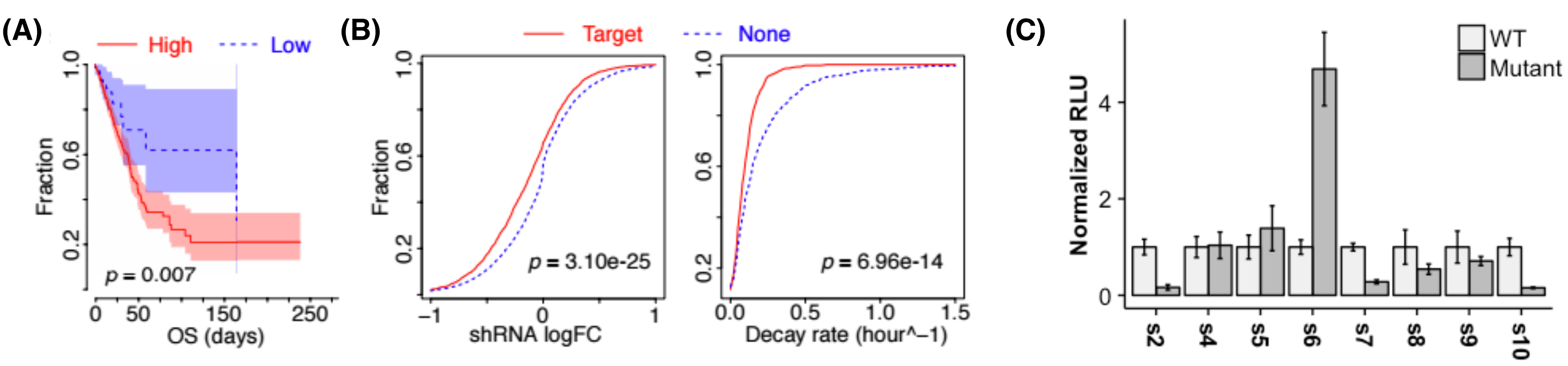
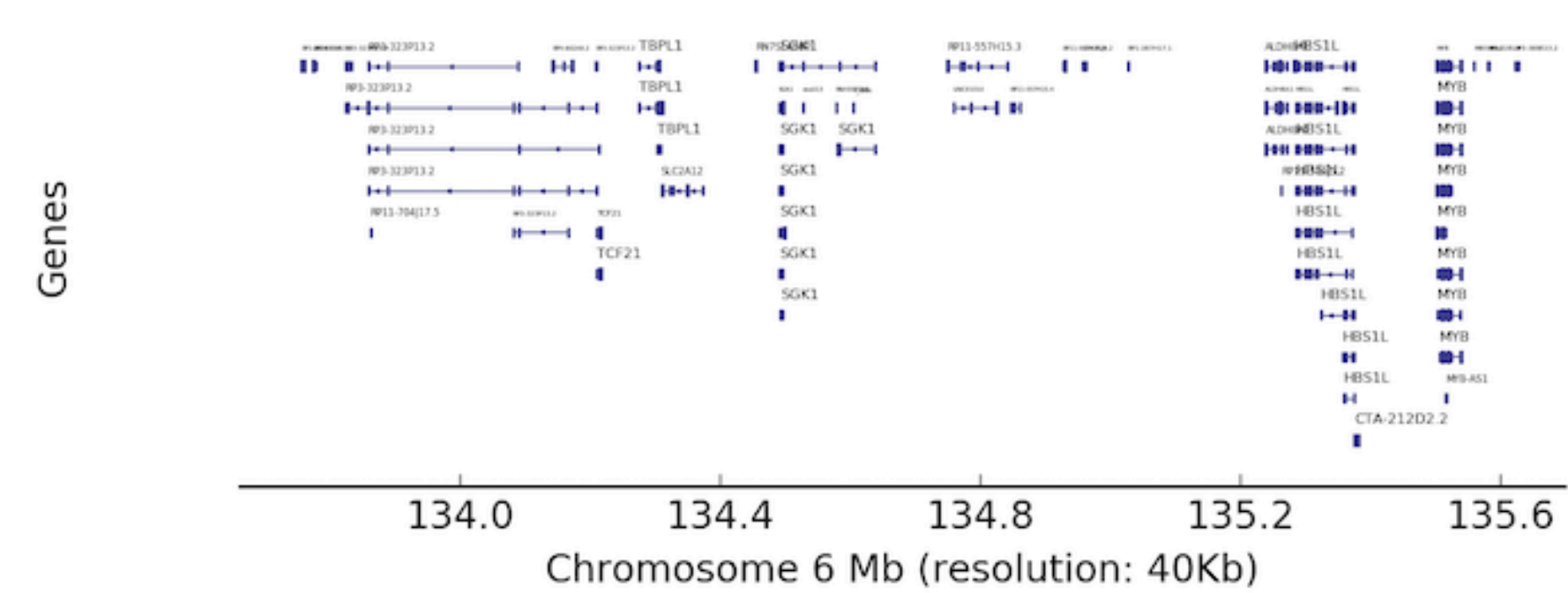
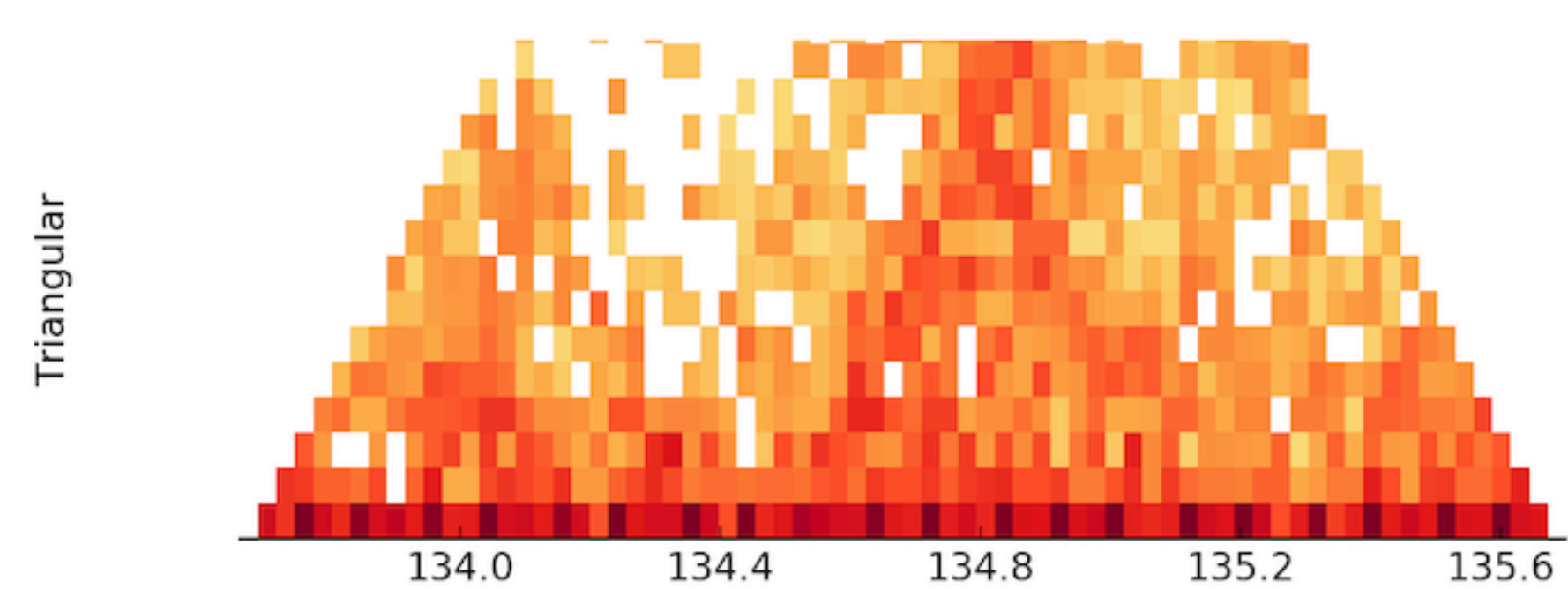
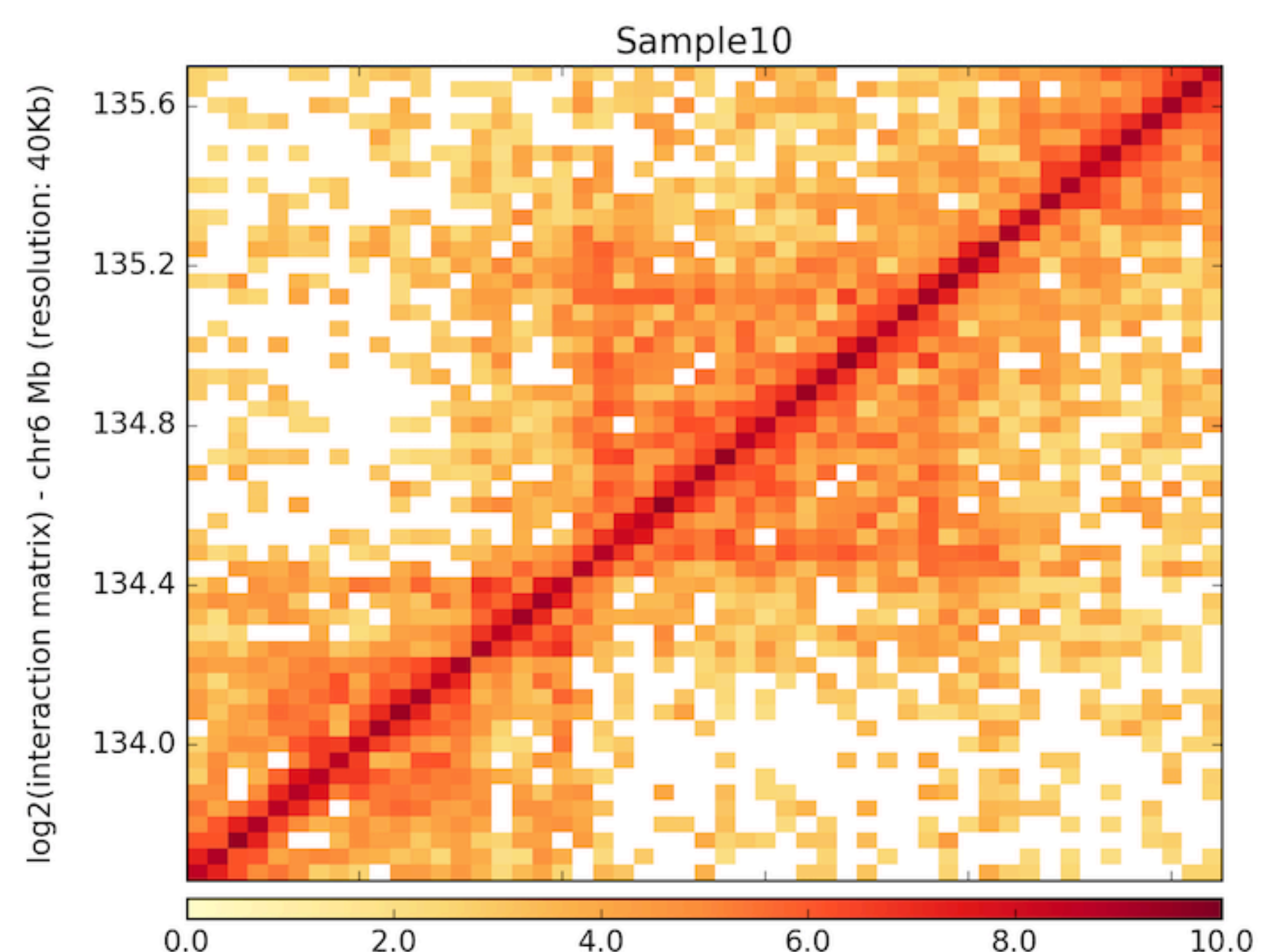
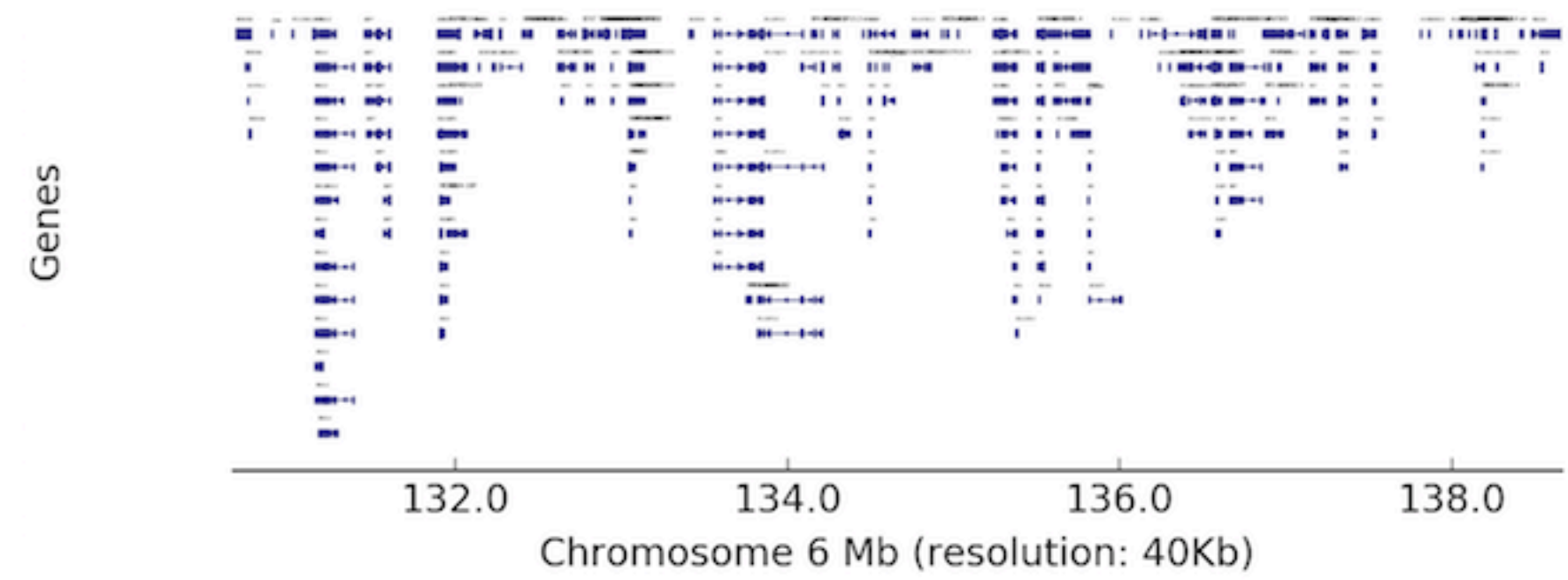
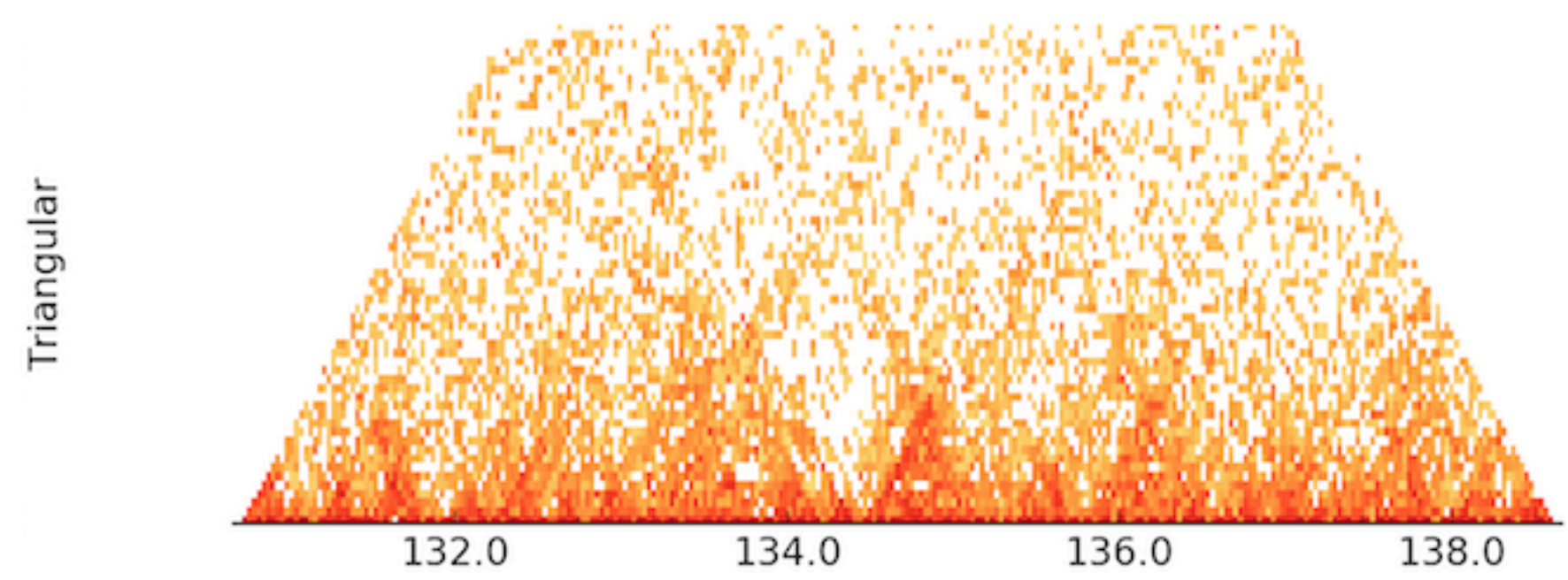
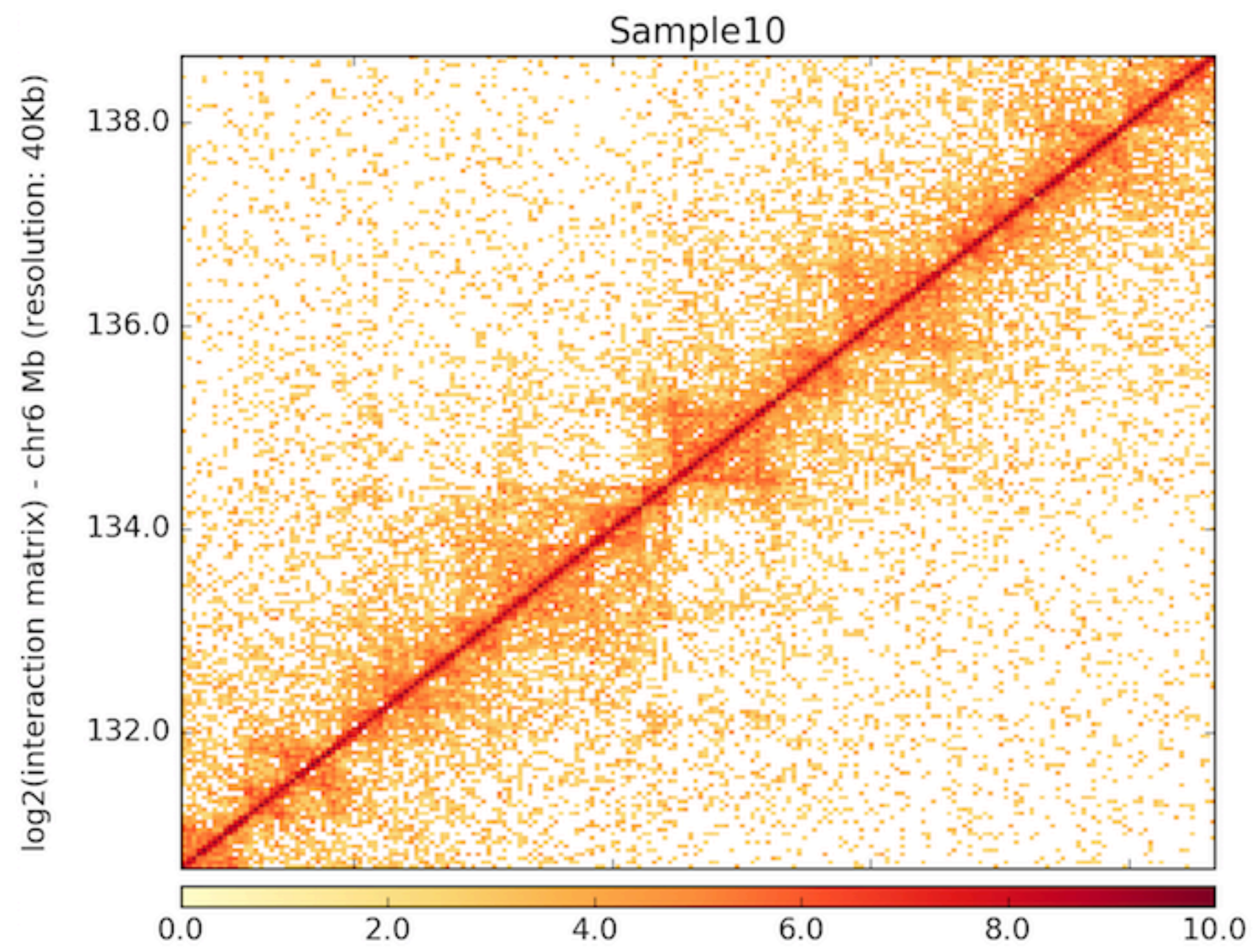
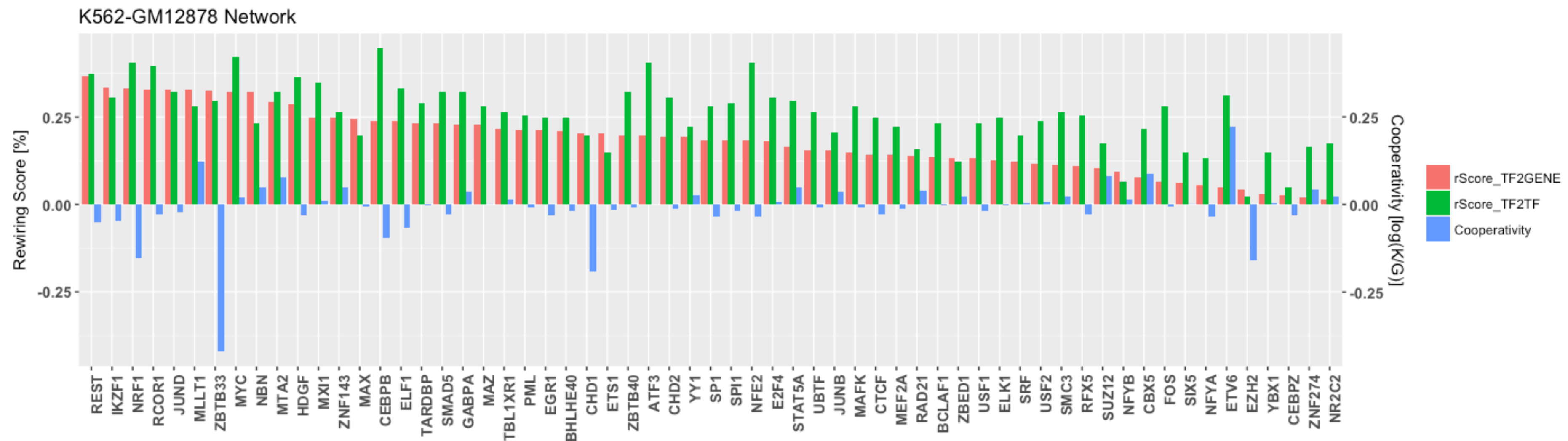


Figure 5



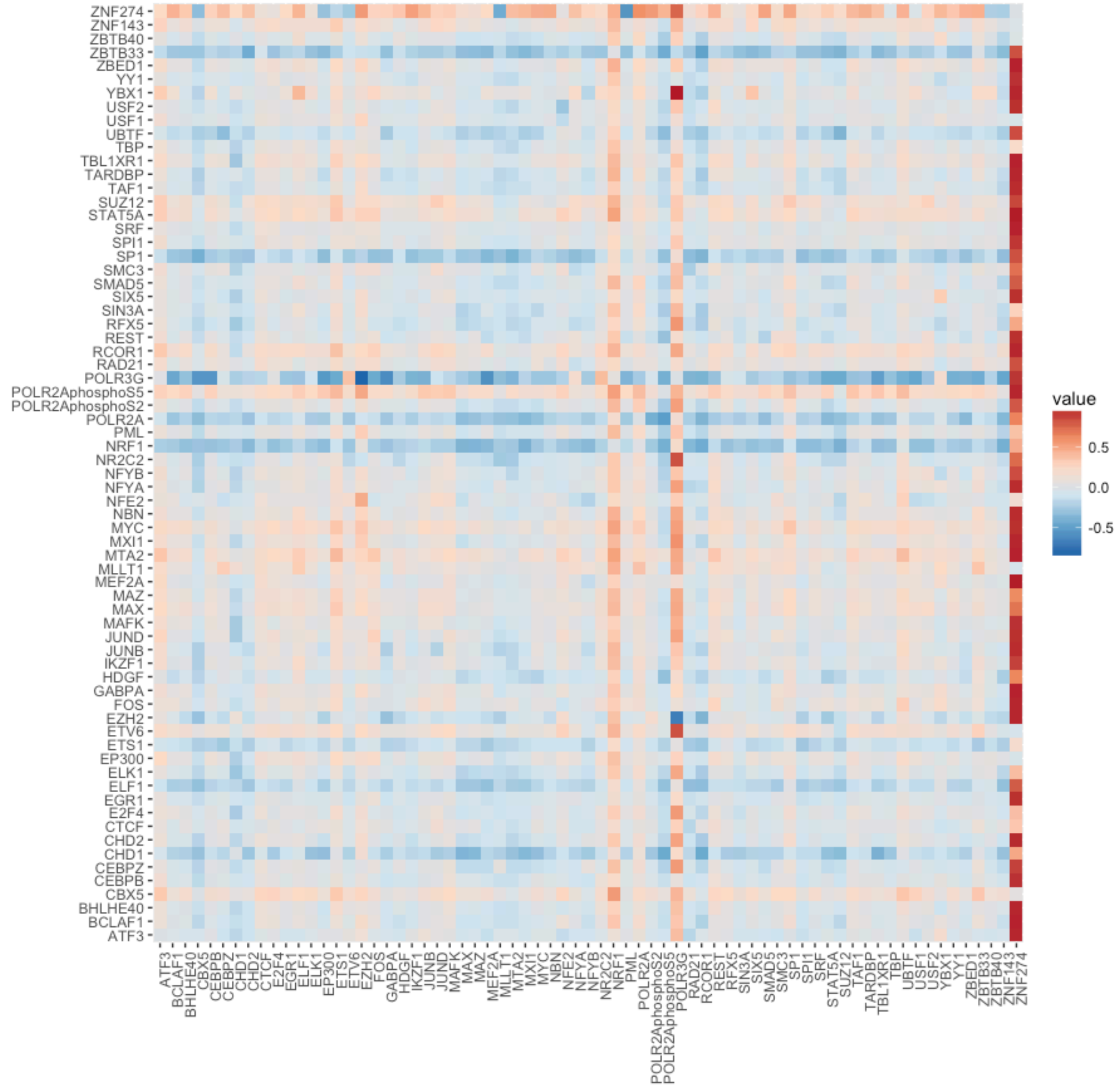
GG's new cooperativity logR of K/G

+ve means it's more cooperative in K, vice versa

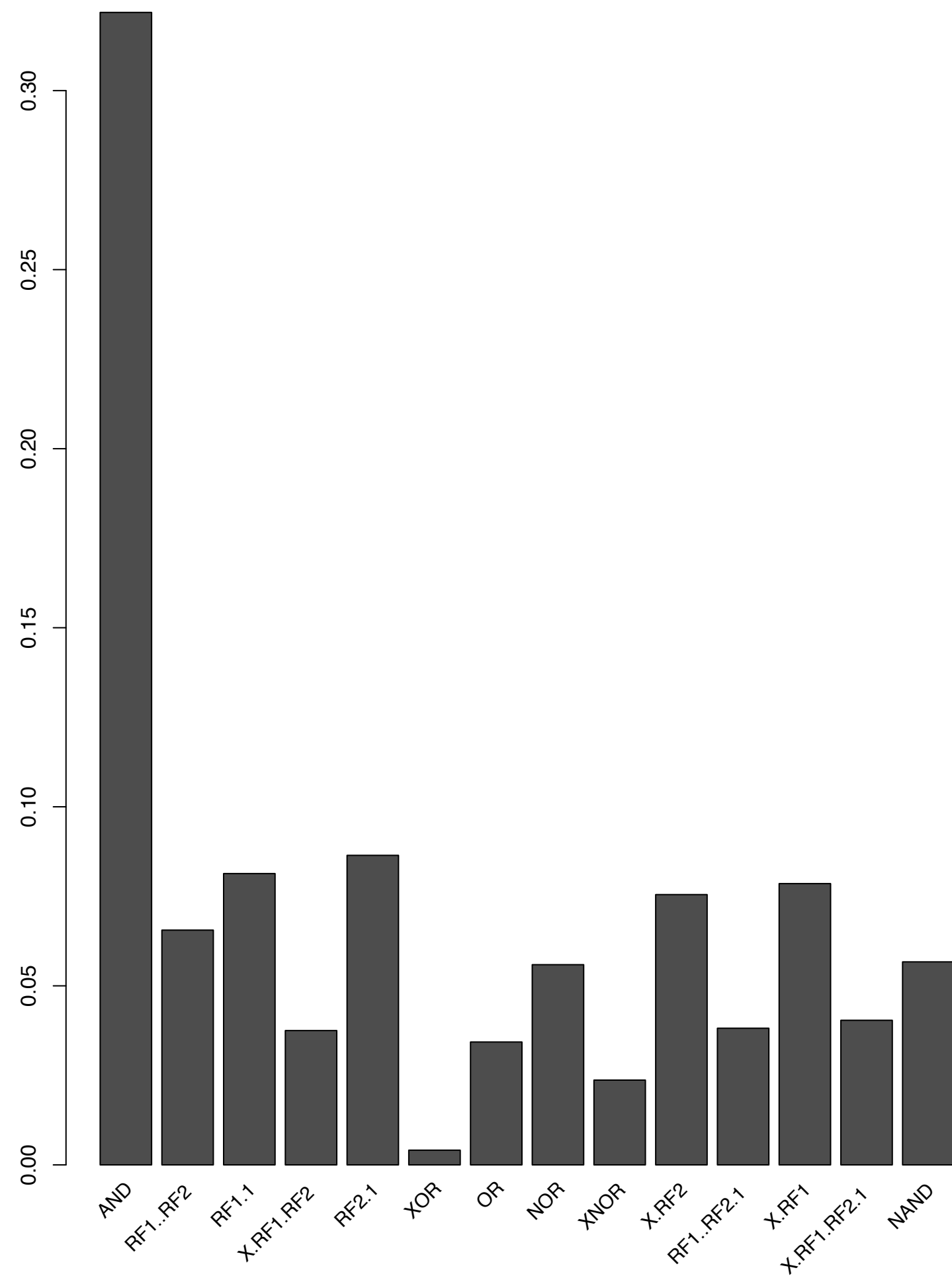


ZBTB33 becomes less cooperative in K
it "could" mean that its targets are unique in K
ETV6 becomes more cooperative in K
this "could" mean they become more ubiquitous

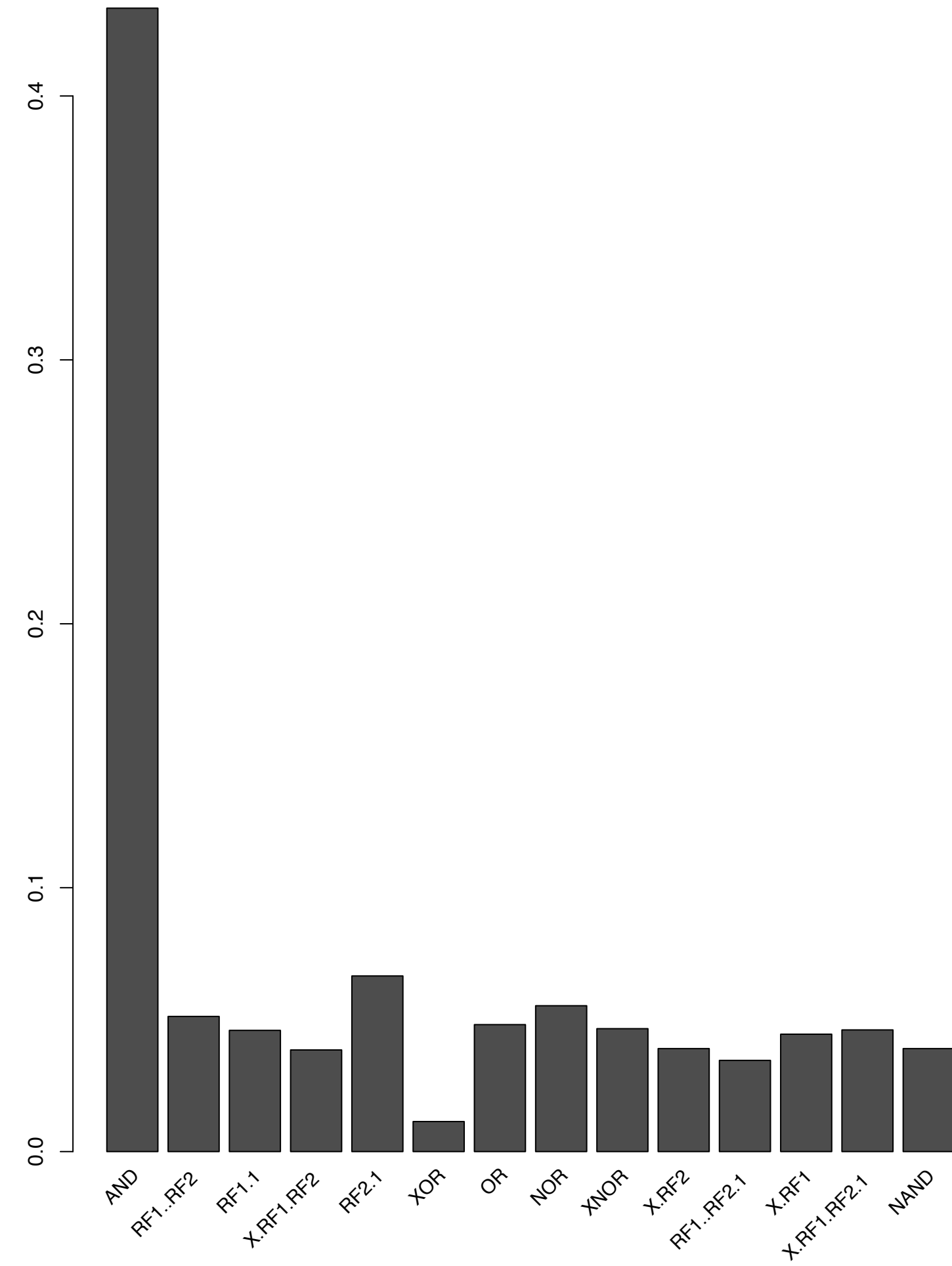
K-G Co-binding



Logic results WITHOUT permutation tests, TIP TF-gene, K&G common TF (without general)



GM12878



K562