

ZENBU-Reports: Supplemental figures

heart CAGE DE TRE

109 heart CAGE libraries on hg38 with gene models and differentially expressed TRE

Differential expression view

This page provide interactive MA plots for Atrium and Ventricle - healthy vs failing comparisons. Data is prefiltered with FDR < 0.1, whole tables are available in supplementary table 9 of the manuscript.

Legend for DE TRE tracks:

- ▶ - failing atrium TRE; ▶ - healthy atrium TRE;
- ▶ - failing ventricle TRE; ▶ - healthy ventricle TRE; ▶ - not DE TRE;

DE TRE - differentially expressed transcribed regulatory elements in heart, FDR < 0.05, $|\log_2FC| > 1$

Legend heart CAGE consensus regions track:

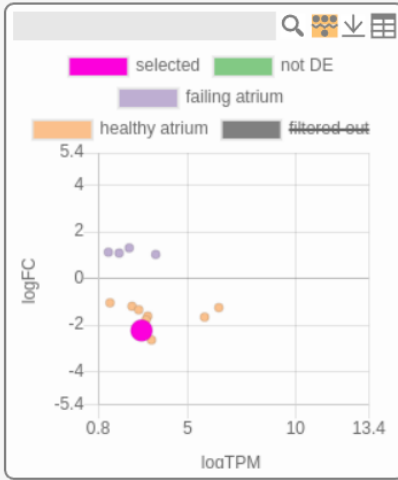
- Encode based: ▶ - promoter; ▶ - proximal enhancer; ▶ - distal enhancer.
- heart CAGE based: ▶ - promoter; ▶ - unidirectional enhancer; ▶ - bidirectional enhancer.

DE TRE in Atrium

DE TRE in Ventricle

cluster_id1	GeneName	tagcounts	location
rDPI_10060	AMOTL1	2337	location
rDPI_40203	C4orf54	3525	location
rDPI_43183	LOC101927046	1938	location
rDPI_4062	LOC105371646	4190	location
rDPI_7990	LOC105376520	7924	location
rDPI_6350	LOC105378351	2259	location
rDPI_7076	LOC107984260	3131	location
rDPI_5131	LOC107985362	1803	location
rDPI_14727	TRAJ49	3655	location
rDPI_19788		410	location
rDPI_6558		26274	location
rDPI_6609		1738	location
rDPI_38875		415	location
rDPI_29970		37779	location

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consensus_regions_class

- enhancer 14
- alternative TSS 19
- promoter 18

localization

- Intron 6
- Distal 5
- Promoter 1

chip_class

- active_enhancer 14
- active_promoter 76
- low signal 16

biotype

- NA 5
- protein_coding 5

search for annotations (eg EGR1 or kinase) or set location (eg: chr19:36373808-36403118) search clear

hg38 chr14 22,489,162-22,489,567+ [len 406bp] 22489352 << < > >> +10x +5x +2x -2x -5x -10x settings export svg

hg38 chr14 22489162..22489567+ [len 406bp]

ENTREZ GENE hg38
GENCODE v37
heart CAGE TRE DE in Atrium
heart CAGE TRE DE in Ventricle
heart CAGE CTSS tracks for healthy vs failing Atrium and Ventricle [rev:0.04 fwd:2.3 scale:2.26] (mean) tagcount_pm
DE: failing_A (15 expts)
DE: failing_V (18 expts)
DE: healthy_A (42 expts)
DE: healthy_V (34 expts)
heart CAGE consensus regions (promoters, enhancers proximal and distal - Encode based)

+ create custom track + add predefined tracks

heart CAGE CTSS tracks for healthy vs failing Atrium and Ven

chr14 22489162..22489567 (406bp) STAT FLT

metadata group [DE] (109 / 109 expts) <- anti-sense strand > sense strand >

- DE: failing_A (15 expts) 0.0331
- DE: failing_V (18 expts) 0.0071
- DE: healthy_A (42 expts) 14.719
- DE: healthy_V (34 expts) 0.1361
- UNKNOWN - no metadata key (0 expts) 0.0

Supplemental Figure 1. ZENBU-Reports page from the Atlas of Heart Promoters and Enhancers (1).

Target subcellular localization

Expression profiling by RNA-seq using cytoplasmic, nuclear soluble, and chromatin-bound RNA was used to measure the relative prevalence of each lncRNA in these three subcellular compartments. The table shows the measured expression in the three compartments for each lncRNA both in counts-per-million ("cpm") and as a percentage value of the relative fraction ("frac"). Based on these values, each lncRNA was assigned to a subcellular compartment as shown in the column "localization". The scatter plots below show pairwise comparisons of the fractional expression values in the three compartments. Data source: Ramiowski JR, et al Genome Research 2020 DOI: [10.1101/gr.254219.119](https://doi.org/10.1101/gr.254219.119); PMID: [32718982](https://pubmed.ncbi.nlm.nih.gov/32718982/); PMCID: [PMC7397864](https://pubmed.ncbi.nlm.nih.gov/PMC7397864/)

Localization

Chromatin bound 20

Cytoplasmic 14

Nuclear soluble 10

FANTOM6 DMFB targets

target	KD_geneID	localization	GSEA	DESeq	MARA	Chr_cpm	Nuc_cpm	Cyt_cpm	Ch
RPL15B.L7.5	ENSG00000216775	Nuclear soluble	GSEA	DESeq	MARA	7.677	13.14	12.98	
RPH1-338L1	ENSG00000245958	Chromatin bound	GSEA	DESeq	MARA	30.26	9.186	5.483	
SNHG18	ENSG00000250786	Nuclear soluble	GSEA	DESeq	MARA	21.68	37.02	17.80	
NNT-AS1	ENSG00000248092	Cytoplasmic	GSEA	DESeq	MARA	7.334	8.695	14.93	
CKMT2-AS1	ENSG00000247572	Chromatin bound	GSEA	DESeq	MARA	18.90	9.441	14.78	
NR2F1-AS1	ENSG00000237187	Chromatin bound	GSEA	DESeq	MARA	49.31	11.37	24.03	
CTC-228N24.3	ENSG00000245837	Chromatin bound	GSEA	DESeq	MARA	112.3	12.34	10.49	
GOS5-AS1	ENSG00000225733	Cytoplasmic	GSEA	DESeq	MARA	13.80	74.01	168.8	
LINC00886	ENSG00000240875	Chromatin bound	GSEA	DESeq	MARA	15.12	6.603	6.310	
TEBC	ENSG00000270141	Nuclear soluble	GSEA	DESeq	MARA	24.69	148.1	20.09	
AC007246.3	ENSG00000231312	Chromatin bound	GSEA	DESeq	MARA	39.62	13.92	17.34	
AC009948.5	ENSG00000223960	Cytoplasmic	GSEA	DESeq	MARA	15.10	13.58	17.95	
ITIL-AS1	ENSG00000237298	Chromatin bound	GSEA	DESeq	MARA	63.41	8.615	10.41	
DNM3OS	ENSG00000230630	Nuclear soluble	GSEA	DESeq	MARA	48.06	54.37	8.942	

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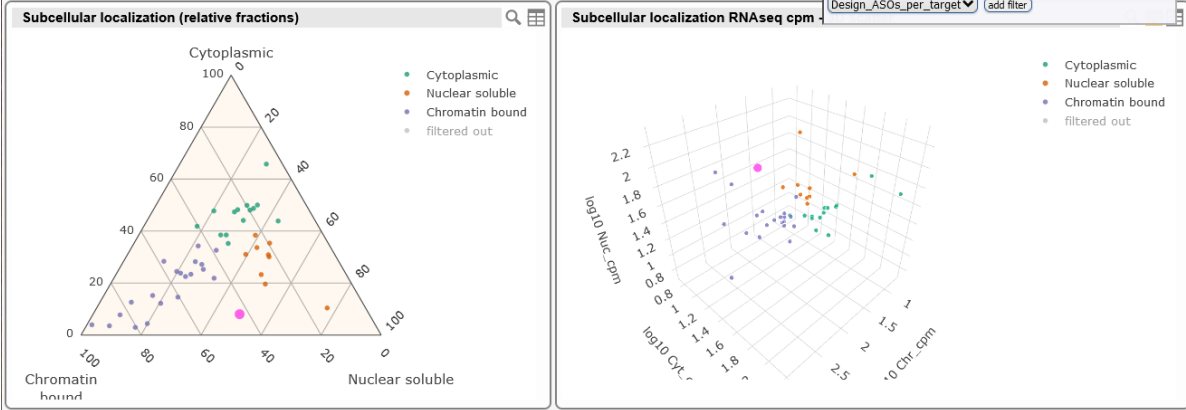
Signal data filters

Chr_cpm absolute value
cutoffs min: 5.00000 max: max

Nuc_cpm absolute value
cutoffs min: 5.00000 max: max

Cyt_cpm absolute value
cutoffs min: 5.00000 max: max

Design_ASOS_per_target



search for annotations (eg EGR1 or kinase) or set location (eg: chr19:36373808-36403118)

hg38 chr1 172,136,449-172,144,876+ [len 8.4kb] [87728163](#)

hg38 chr1 172136449..172144876+ [len 8.428kb]

Ensembl gene hg38

DMN3OS

MIR214

MIR3120

MIR199A2

[Gene model] FANTOM6 CAT gene info [rev:2. fvd:31] (mean) numPmtmr

CATG00000082745

CATG00000025347

30

ENSG00000208024

[Gene model] GENCODEv25, transcripts

F6 HDF ASO: CAGE signal KD-ref (runs 1-21) - 20170223

F6 HDF: RNA-seq

F6 HDF ASO: CAT TSS merged promoters regions with HDF CAGE signal (runs 1-21) - 20170223 - group by KD target

F6 HDF: set1 lncRNA target transcript

F6 HDF: adHoc; DMFB_ASO_1ffover_from_hg19_to_hg38; batich1_to_9_exlon

G0230630|ENSG00000230630:1|ENST00000417354:1

DMFB qPCR primers (n=900), paired, hg38, (fflcover from hg19)

DMFB qPCR primers (n=900), single, hg38, (fflcover from hg19)

F6 HDF: fractionation RNAseq (rev:2.0 fvd:0.06 scale:2.05) (mean) tpm

fraction: chromatin (2 exps)

fraction: cytoplasmic (2 exps)

fraction: nuclear (2 exps)

F6 HDF : fractionation RNAseq

metadata group [fraction] (6 / 6 exps)

- fraction: chromatin (2 exps)
- fraction: cytoplasmic (2 exps)
- fraction: nuclear (2 exps)
- UNKNOWN - no metadata key (0 exps)

chr1 172136449..172144876 (8.4kb) [STAT] [ELT]

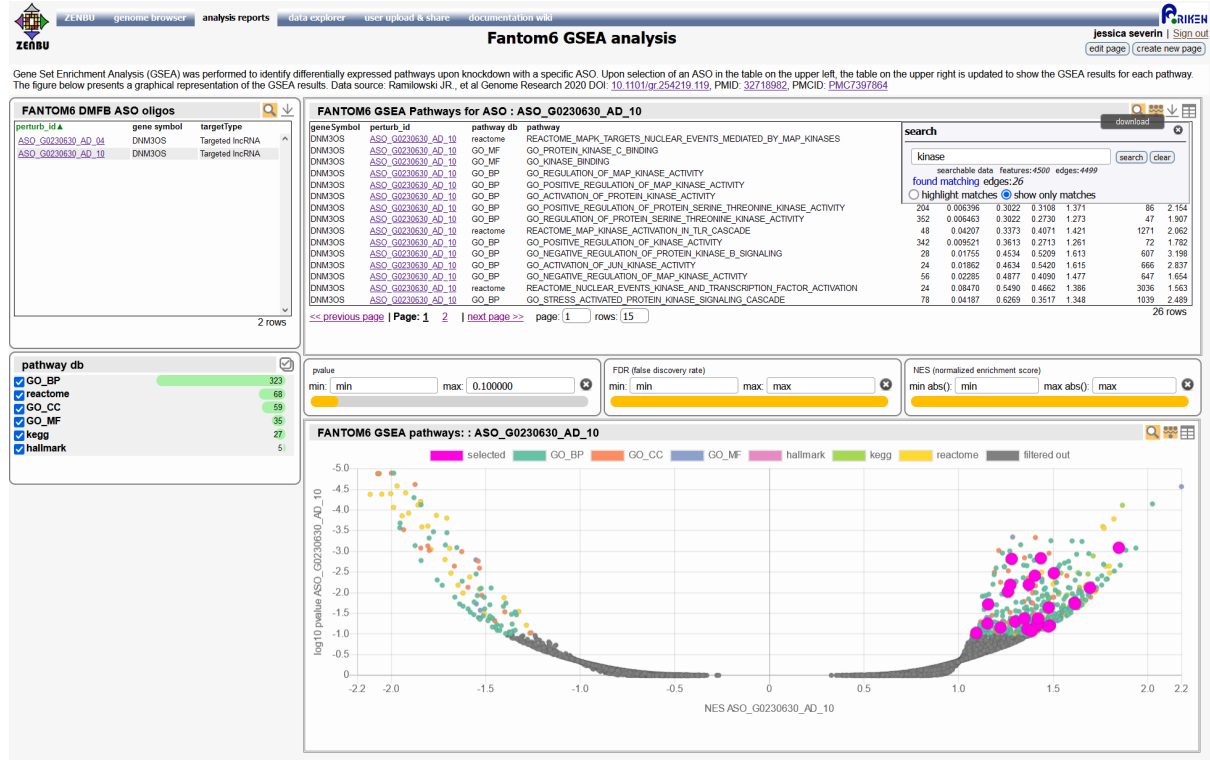
<- anti-sense strand > sense strand ->

30.291 11.76

4.72 10.21

19.807 11.6

Supplemental Figure 2. ZENBU-Reports page showing subcellular localization data of lncRNAs included in FANTOM6 (2).



Supplemental Figure 3. Gene Set Enrichment Analysis results obtained in FANTOM6 (2),

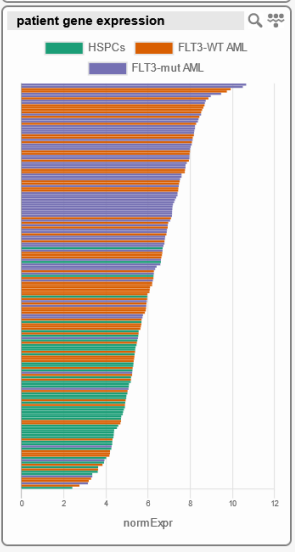
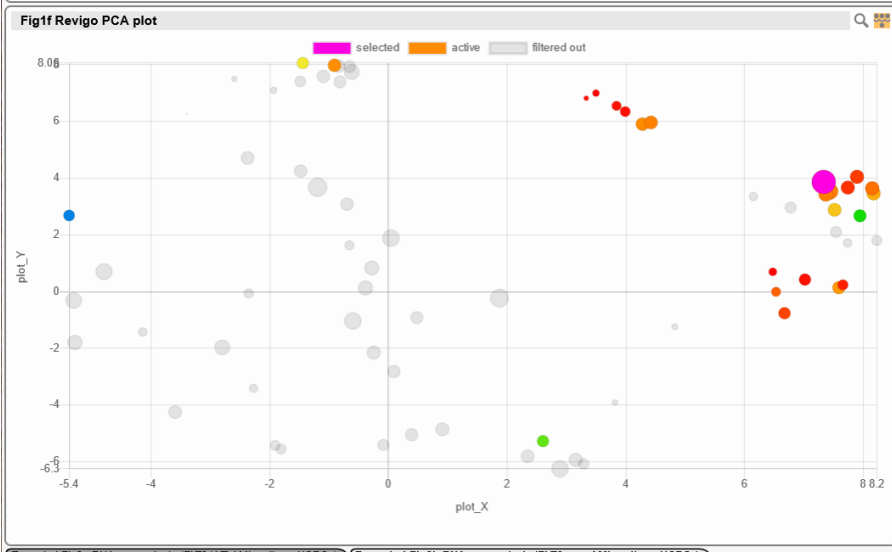
Identification of therapeutic targets in high-risk poor-outcome AML patients

Fig1f Revigo data										
description	term_ID	log10_p-value	uniqueness	dispensability	frequency	representative	eliminated	plot_size	plot_X	plot_Y
immune effector process	GO:0002252	-18.18	0.6740	0	0.1500	2252	0	4.375	-5.384	2.686
regulation of multicellular organismal process	GO:0051239	-12.93	0.6740	0.2440	0.6300	51239	0	4.906	7.947	2.674
cell migration	GO:0016477	-11.82	0.7380	0.2570	0.2900	16477	0	4.575	2.604	-5.273
response to external biotic stimulus	GO:0043207	-9.483	0.7290	0.3360	0.3000	43207	0	4.585	-1.443	8.059
regulation of developmental process	GO:0050793	-8.149	0.6830	0.2790	1.210	50793	0	5.189	7.519	2.905
regulation of cell proliferation	GO:0042127	-7.939	0.7570	0.2350	0.3100	42127	0	4.603	7.336	3.966
positive regulation of biological process	GO:0048518	-7.225	0.7620	0.3130	1.740	48518	0	5.350	8.176	3.466
leukocyte activation involved in inflammatory response	GO:0002269	-6.777	0.6630	0.4630	0	2269	0	0.4770	-3.397	6.258
regulation of localization	GO:0032879	-6.400	0.7440	0.2830	0.7300	32879	0	4.969	7.591	0.1400
response to organic substance	GO:0010033	-6.230	0.7580	0.4740	0.9000	10033	0	5.062	-0.9100	7.980

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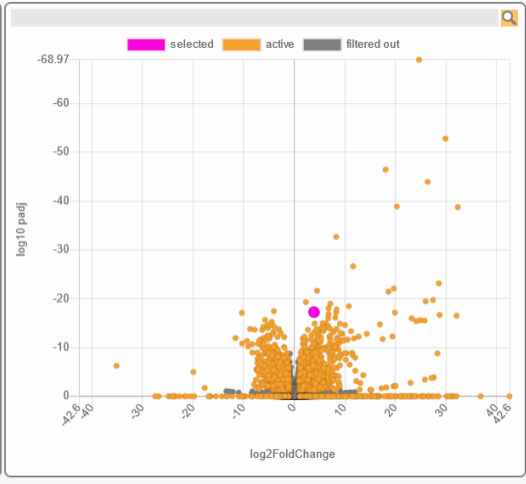
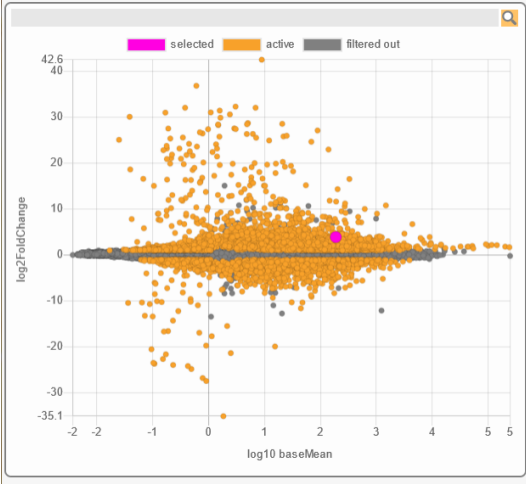
GOterm expressed genes		
term_ID	geneName	baseMean
GO:0042127	HOXD13	0.9688
GO:0042127	HP1BP3	1043
GO:0042127	ERS	158.8
GO:0042127	L4R	88.40
GO:0042127	NHA	0.9944
GO:0042127	JAG1	188.4
GO:0042127	JAG2	3.565
GO:0042127	JUN	830.9
GO:0042127	JUNB	389.9

167 rows



Extended Fig2a RNAseq analysis (FLT3-WT AML cells vs HSPCs)							
geneName	baseMean	log2FoldChange	padj	pvalue	stat	lfcSE	
JAG1	188.4	3.903	5.750e-18	6.530e-21	9.381	0.4160	

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Supplemental Figure 4. ZENBU-Reports page providing an interactive PCA plot showing potential therapeutic targets for the treatment of Acute Myeloid Leukemia (3).

Bibliography

1. Deviatiiarov,R.M., Gams,A., Kulakovskiy,I.V., Buyan,A., Meshcheryakov,G., Syunyaev,R., Singh,R., Shah,P., Tatarinova,T.V., Gusev,O., *et al.* (2023) An atlas of transcribed human cardiac promoters and enhancers reveals an important role of regulatory elements in heart failure. *Nat. Cardiovasc. Res.*, doi: 10.1038/s44161-022-00182-x.
2. Ramilowski,J.A., Yip,C.W., Agrawal,S., Chang,J.-C., Ciani,Y., Kulakovskiy,I.V., Mendez,M., Ooi,J.L.C., Ouyang,J.F., Parkinson,N., *et al.* (2020) Functional annotation of human long noncoding RNAs via molecular phenotyping. *Genome Res.*, **30**, 1060–1072.
3. Hashimoto,M., Saito,Y., Nakagawa,R., Ogahara,I., Takagi,S., Takata,S., Amitani,H., Endo,M., Yuki,H., Ramilowski,J.A., *et al.* (2021) Combined inhibition of XIAP and BCL2 drives maximal therapeutic efficacy in genetically diverse aggressive acute myeloid leukemia. *Nat. Cancer*, **2**, 340–356.