Beside enrichTF (BioC), MEME, HOMER is another packages to compute the TF enrichment. I have preferred to use HOMER due to its increased popularity.

HOMER computes:

- Enrichment of known TF motifs (slide2)
- De Novo TF motif finding (slide3)

Considering the ~1889 genes that are liver-specific, we have computed the TF enrichment in their promoters.

As shown on the next two slides, HOMER identifies:

- The typical (generic) promoters motifs that are not-gene specific, where the general transcription machinery binds; TATA-Box, NFY/CAAT motifs.
- Liver specific promoter motifs, particularly SP and KLF transcription factors. The functions of these TF in liver physiology and pathology have been well substantiated (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10003758/)
- Very interestingly, de novo motif analysis highlights HNF1B (hepatocyte nuclear factor-1 beta)

Enrichment of known TF motifs

Homer Known Motif Enrichment Results (df4.pc.samples.of.interest.txt.liver.specific.genes.txt.liver.specific.genes.TSS.motifs)

Homer de novo Motif Results Gene Ontology Enrichment Results Known Motif Enrichment Results (txt file) Total Target Sequences = 1890, Total Background Sequences = 47601						
Rank Motif	Name	P- value	log P- pvalue	q-value (Benjamini)	# Target Sequences with Motif	% of Targets Sequences with Motif
¹ <u><u><u><u><u></u><u><u><u></u><u><u><u></u><u><u><u></u><u><u><u></u></u> <u><u></u> <u><u></u> <u><u></u> <u><u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u></u>	Sp5(Zf)/mES-Sp5.Flag-ChIP-Seq(GSE72989)/Homer	1e-90	-2.078e+02	0.0000	1002.0	53.02%
² EFGGGFGGGG	KLF1(Zf)/HUDEP2-KLF1-CutnRun(GSE136251)/Homer	1e-84	-1.956e+02	0.0000	888.0	46.98%
3 SCCCCCCCE	Sp1(Zf)/Promoter/Homer	1e-83	-1.929e+02	0.0000	619.0	32.75%
4 ACCCAATESE	NFY(CCAAT)/Promoter/Homer	1e-75	-1.748e+02	0.0000	363.0	19.21%
· FECCOCCC	Sp2(Zf)/HEK293-Sp2.eGFP-ChIP-Seq(Encode)/Homer	1e-75	-1.748e+02	0.0000	1146.0	60.63%
· EFECCECCETEE	KLF3(Zf)/MEF-Klf3-ChIP-Seq(GSE44748)/Homer	1e-67	-1.557e+02	0.0000	584.0	30.90%
⁷ EGGGEGEG	KLF5(Zf)/LoVo-KLF5-ChIP-Seq(GSE49402)/Homer	1e-64	-1.494e+02	0.0000	992.0	52.49%
* EGTCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	KLF14(Zf)/HEK293-KLF14.GFP-ChIP-Seq(GSE58341)/Homer	1e-56	-1.310e+02	0.0000	1196.0	63.28%
PRICE STREET FOR THE PRICE STR	KLF6(Zf)/PDAC-KLF6-ChIP-Seq(GSE64557)/Homer	1e-54	-1.253e+02	0.0000	842.0	44.55%
¹⁰ GCCACACCCCACE	Klf9(Zf)/GBM-Klf9-ChIP-Seq(GSE62211)/Homer	1e-35	-8.276e+01	0.0000	404.0	21.38%
" GCCACACCCA	Klf4(Zf)/mES-Klf4-ChIP-Seq(GSE11431)/Homer	1e-24	-5.729e+01	0.0000	272.0	14.39%
12 GGGGTGTGTG	KLF10(Zf)/HEK293-KLF10.GFP-ChIP-Seq(GSE58341)/Homer	1e-22	-5.207e+01	0.0000	310.0	16.40%
13 GGGGGGGG	Maz(Zf)/HepG2-Maz-ChIP-Seq(GSE31477)/Homer	1e-22	-5.156e+01	0.0000	946.0	50.05%
14 CCTTTTATAGES	TATA-Box(TBP)/Promoter/Homer	1e-17	-4.086e+01	0.0000	220.0	11.64%

De Novo TF motif finding and enrichment

Homer de novo Motif Results (df4.pc.samples.of.interest.txt.liver.specific.genes.txt.liver.specific.genes.TSS.motifs/

Known Motif Enrichment Results

Gene Ontology Enrichment Results

If Homer is having trouble matching a motif to a known motif, try copy/pasting the matrix file into <u>STAMP</u> More information on motif finding results: <u>HOMER | Description of Results | Tips</u>

Total target sequences = 1890

Total background sequences = 47607

* - possible false positive

_	Motif	P-value	log P-pvalue	% of Targets	% of Background	STD(Bg STD)	Best Match/Details	Motif File
1	FECCCOCCE	1e-96	-2.213e+02	46.77%	24.59%	49.2bp (57.5bp)	Sp2(Zf)/HEK293-Sp2.eGFP-ChIP-Seq(Encode)/Homer(0.964) More Information Similar Motifs Found	motif file (matrix)
2	CECE ATTOCK	1e-82	-1.891e+02	15.08%	3.92%	53.7bp (59.9bp)	NFY(CCAAT)/Promoter/Homer(0.967) More Information Similar Motifs Found	motif file (matrix)
3	CECTTITATA	1e-22	-5.273e+01	3.86%	0.92%	46.2bp (62.5bp)	TBP/MA0108.2/Jaspar(0.857) More Information Similar Motifs Found	motif file (matrix)
4	SETTAATEATTA	1e-20	-4.826e+01	1.11%	0.05%	52.0bp (54.2bp)	HNF1b(Homeobox)/PDAC-HNF1B-ChIP-Seq(GSE64557)/Homer(0.931) More Information Similar Motifs Found	motif file (matrix)
5	TGACGICATA	1e-20	-4.764e+01	7.94%	3.35%	50.2bp (57.0bp)	Atf1(bZIP)/K562-ATF1-ChIP-Seq(GSE31477)/Homer(0.923) More Information Similar Motifs Found	motif file (matrix)
6	CIACAAITCC	1e-18	-4.284e+01	2.80%	0.61%	45.8bp (63.4bp)	GFY(?)/Promoter/Homer(0.891) More Information Similar Motifs Found	motif file (matrix)
7	<u>AGTCACGTGA</u>	1e-16	-3.804e+01	8.99%	4.48%	50.0bp (55.0bp)	TFE3(bHLH)/MEF-TFE3-ChIP-Seq(GSE75757)/Homer(0.924) More Information Similar Motifs Found	motif file (matrix)
8	TACTTCCGTT	1e-15	-3.485e+01	18.73%	12.29%	54.3bp (61.0bp)	ELK3/MA0759.1/Jaspar(0.825) More Information Similar Motifs Found	motif file (matrix)
9	<u>ACTTICACTTIC</u>	1e-15	-3.473e+01	1.22%	0.12%	35.2bp (58.6bp)	IRF1(IRF)/PBMC-IRF1-ChIP-Seq(GSE43036)/Homer(0.946) More Information Similar Motifs Found	motif file (matrix)
10	ACCAGGEAGTIE	1e-14	-3.296e+01	3.02%	0.88%	53.1bp (58.6bp)	ELF3(ETS)/PDAC-ELF3-ChIP-Seq(GSE64557)/Homer(0.842) More Information Similar Motifs Found	motif file (matrix)
11	CTTTAAAGGG	1e-14	-3.295e+01	8.78%	4.59%	50.7bp (63.8bp)	TATA-Box(TBP)/Promoter/Homer(0.711) More Information Similar Motifs Found	motif file (matrix)