

## Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see [Authors & Referees](#) and the [Editorial Policy Checklist](#).

### Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a Confirmed

- The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement
- An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- The statistical test(s) used AND whether they are one- or two-sided  
*Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
- A description of all covariates tested
- A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
- For null hypothesis testing, the test statistic (e.g.  $F$ ,  $t$ ,  $r$ ) with confidence intervals, effect sizes, degrees of freedom and  $P$  value noted  
*Give  $P$  values as exact values whenever suitable.*
- For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- Estimates of effect sizes (e.g. Cohen's  $d$ , Pearson's  $r$ ), indicating how they were calculated
- Clearly defined error bars  
*State explicitly what error bars represent (e.g. SD, SE, CI)*

*Our web collection on [statistics for biologists](#) may be useful.*

### Software and code

Policy information about [availability of computer code](#)

Data collection

The Illumina bcl2fastq tool was used to process raw sequencing basecalls from Illumina sequencer machines (HiSeq 2500, HiSeq4000 and NextSeq 500).

Data analysis

BaMM motif and gkm-SVM were both run with default parameters. We used the latest version of the larger scale gkm-SVM, LS-GKM (compiled from source code downloaded from <https://github.com/Dongwon-Lee/lsgkm> on 8/25/16), and BaMM motif (v1.0 downloaded from [github.com/soedinglab/BaMMmotif](https://github.com/soedinglab/BaMMmotif)). Both models were trained using five-fold cross validation. Model performance was scored using `roc_auc_score` and `precision_score` functions from the `metrics` module of `sklearn`.

Other analysis were performed using Python (with the packages - `numpy`, `pandas`, `sklearn`, `matplotlib`, `seaborn`, `scipy`, `Biopython`). The source code for our model is available at: <https://github.com/jenhantao/tba>

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [guidelines for submitting code & software](#) for further information.

## Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Data generated for this study has been deposited to the NCBI Gene Expression Omnibus (GEO) under the accession number GSE111856

## Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences  Behavioural & social sciences  Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/authors/policies/ReportingSummary-flat.pdf](https://www.nature.com/authors/policies/ReportingSummary-flat.pdf)

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sequencing experiments were done in duplicate
Data exclusions	AP-1 family members were excluded by ChIP-sequencing based on low peak counts or quality.
Replication	Reproducibility of sequencing data was performed by IDR (Irreproducibile discovery rate).
Randomization	Randomization was not relevant to this study
Blinding	Blinding was not possible for this study

## Reporting for specific materials, systems and methods

### Materials & experimental systems

n/a	Involvement in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Unique biological materials
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants

### Methods

n/a	Involvement in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Antibodies

Antibodies used

Fos Rabbit polyclonal Santa Cruz sc-7202  
 FosL1 Rabbit polyclonal Santa Cruz sc-605  
 FosL2 Mouse monoclonal Santa Cruz sc-166102  
 Fosb Rabbit polyclonal Cell Signaling 2251  
 Jun Rabbit polyclonal Santa Cruz sc-1694  
 Jun Mouse monoclonal Santa Cruz sc-74543  
 JunB Rabbit polyclonal Santa Cruz sc-73  
 JunD Rabbit polyclonal Santa Cruz sc-74  
 Jdp2 Rabbit polyclonal Thermo PA5-19692  
 Batf Rabbit polyclonal Brookwood Biomedical PAB4003  
 Batf2 Rabbit polyclonal Santa Cruz sc-241891  
 Batf3 Rabbit polyclonal Abnova H00055509-M04  
 C/ebp Rabbit polyclonal Santa Cruz sc-61  
 Pu.1 Rabbit polyclonal Santa Cruz sc-352

PPARg Rabbit polyclonal Santa Cruz sc-7196  
 PPARg Rabbit monoclonal Cell Signaling C26H12  
 PPARg Rabbit polyclonal Diagenode C15410133

## Validation

All antibodies were tested by the manufacturers using Western Blot, ChIP, or both.

Methods for each specific antibody are as follows:  
 Reactivity,Description,Company,Catalog #, Validation Method  
 ATF2,Rabbit polyclonal,Santa Cruz,sc-187,ChIP  
 Atf3,Rabbit polyclonal,Thermo,PA5-41308,Western  
 Atf3,Rabbit polyclonal,Thermo,PA5-36244,ChIP  
 Atf4,Rabbit polyclonal,Cell Signaling,11815,ChIP  
 Atf4,Rabbit polyclonal,Sigma,ABE387,ChIP  
 Fos,Rabbit polyclonal,Santa Cruz,sc-7202,Western/ChIP  
 FosL1,Rabbit polyclonal,Santa Cruz,sc-605,ChIP  
 FosL2,Mouse monoclonal,Santa Cruz,sc-166102,Western/ChIP  
 Fosb,Rabbit polyclonal,Cell Signaling,2251,ChIP  
 Jun,Rabbit polyclonal,Santa Cruz,sc-1694,ChIP  
 Jun,Mouse monoclonal,Santa Cruz,sc-74543,Western  
 JunB,Rabbit polyclonal,Santa Cruz,sc-73,Western/ChIP  
 JunD,Rabbit polyclonal,Santa Cruz,sc-74,Western/ChIP  
 Jdp2,Rabbit polyclonal,Thermo,PA5-19692,ChIP  
 Batf,Rabbit polyclonal,Brookwood Biomedical,PAB4003,ChIP  
 Batf2,Rabbit polyclonal,Santa Cruz,sc-241891,ChIP  
 Batf3,Rabbit polyclonal,Abnova,H00055509-M04,ChIP  
 C/ebp,Rabbit polyclonal,Santa Cruz,sc-61,ChIP  
 Pu.1,Rabbit polyclonal,Santa Cruz,sc-352,ChIP  
 PPARg,Rabbit polyclonal,Santa Cruz,sc-7196,ChIP/IP  
 PPARg,Rabbit monoclonal,Cell Signaling,C26H12,ChIP/IP  
 PPARg,Rabbit polyclonal,Diagenode,C15410133,ChIP/IP

## Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

## Laboratory animals

C57Bl/6EiJ/ Male/ 8-10 weeks; Balbc/J/Male/8-10 weeks/ ; PPARgamma-MXCre-lysMCre(

## Wild animals

No wild animals were used for this study

## Field-collected samples

No field collected samples were used for this study

## ChIP-seq

### Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).  
 Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

## Data access links

*May remain private before publication.*

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE111856>

## Files in database submission

ChIP-seq Files:  
 Balbc\_Thiomac\_ChIP\_ATF3\_KLA-1h\_GJF\_16-07-25.fastq.gz  
 Balbc\_Thiomac\_ChIP\_ATF3\_KLA-1h\_GJF\_16-08-16-rep1.fastq.gz  
 Balbc\_Thiomac\_ChIP\_ATF3\_Veh\_GJF\_16-08-16.fastq.gz  
 Balbc\_Thiomac\_ChIP\_ATF3\_Veh\_GJF\_16-08-16-rep1.fastq.gz  
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 Balbc\_Thiomac\_ChIP\_cJun\_Veh\_GFEW\_10-19-15.fastq.gz  
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 C57Bl6-JunKO-Atf3DBD\_iBMDM\_ChIP\_Veh\_peaks.tsv

Genome browser session  
 (e.g. [UCSC](https://genome.ucsc.edu))

[https://genome.ucsc.edu/cgi-bin/hgTracks?db=mm10&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&position=chr2%3A91111792%2D91130873&hgslid=691425423\\_PcaidXtMcJWKMDrZtVhQbx5ANm3f](https://genome.ucsc.edu/cgi-bin/hgTracks?db=mm10&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&position=chr2%3A91111792%2D91130873&hgslid=691425423_PcaidXtMcJWKMDrZtVhQbx5ANm3f)

## Methodology

Replicates

ChIP-seq experiments were performed using two biological replicates.

Sequencing depth

All experiments were sequenced using single-end sequencing with 50 basepair reads. Sequencing depth information is as follows:

sample,totalReads,uniquelyMappedReads  
 C57Bl6\_Thiomac\_ChIP\_ATF3\_KLA-1h\_GJF\_16-04-21,20832779,15944758  
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 C57Bl6\_Thiomac\_ChIP\_CEBPa\_KLA-1h\_GFEW\_15-11-18,13195714,9503237  
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 C57Bl6\_Thiomac\_ChIP\_CEBPa\_Veh\_GJF\_16-06-14,23465571,16824200  
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 Balbc\_Thiomac\_ChIP\_JunB\_KLA-1h\_GJF\_16-10-13,33235992,21246092  
 Balbc\_Thiomac\_ChIP\_JunB\_Veh\_GFEW\_10-19-15,16893268,12257203  
 Balbc\_Thiomac\_ChIP\_JunB\_Veh\_GJF\_16-07-22,36659682,21313858  
 Balbc\_Thiomac\_ChIP\_JunD\_KLA-1h\_GFEW\_10-19-15,23177438,18589699  
 Balbc\_Thiomac\_ChIP\_JunD\_KLA-1h\_GJF\_16-10-13,16793235,12392873  
 Balbc\_Thiomac\_ChIP\_JunD\_Veh\_GFEW\_10-19-15,17053352,13166237  
 Balbc\_Thiomac\_ChIP\_JunD\_Veh\_GJF\_16-06-12,18132403,13994506  
 Balbc\_Thiomac\_ChIP\_p65\_KLA-1h\_GJF\_16-07-25-rep1,23411560,18636794  
 Balbc\_Thiomac\_ChIP\_p65\_KLA-1h\_GJF\_16-08-16,18893355,14639153  
 Balbc\_Thiomac\_ChIP\_p65\_Veh\_GJF\_16-07-22-rep1,20011412,14203439  
 Balbc\_Thiomac\_ChIP\_p65\_Veh\_GJF\_16-07-22-rep2,22364065,17296430  
 Balbc\_Thiomac\_ChIP\_PU1\_KLA-1h\_GFEW\_10-19-15,51135494,42271859  
 Balbc\_Thiomac\_ChIP\_PU1\_KLA-1h\_GJF\_16-06-12,11670965,8831119  
 Balbc\_Thiomac\_ChIP\_PU1\_Veh\_GFEW\_10-19-15,22315429,17907846  
 Balbc\_Thiomac\_ChIP\_PU1\_Veh\_GJF\_16-06-12,15152742,12503148  
 C57Bl6-negAtf3KOAtf3DBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep1,23194439,14854197  
 C57Bl6-negAtf3KOAtf3DBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep2,12585875,8522448  
 C57Bl6-negAtf3KOFosDBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep1,12998513,8788737  
 C57Bl6-negAtf3KOFosDBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep2,13953195,9190279  
 C57Bl6-negAtf3KJunDBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep1,14775525,10263483  
 C57Bl6-negAtf3KJunDBD\_iBMDM\_ChIP\_ATF3\_Veh\_GJF\_18-02-20-rep2,19700906,13170127  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_ATF3\_Veh\_GJF\_16-07-23-1,17657968,13234402  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_ATF3\_Veh\_GJF\_16-07-23-2,20526757,15981630  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_cJun\_Veh\_GJF\_16-07-23-2,19364962,13422113  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_cJun\_Veh\_GJF\_16-08-16,7057133,4813601  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_Fos\_Veh\_GJF\_16-07-23-1,24672506,17633503  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_Fos\_Veh\_GJF\_16-07-23-2,17824003,12828075  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_JunD\_Veh\_GJF\_16-07-23-1,19775947,14657301  
 C57Bl6-PPARgKO\_Thiomac\_ChIP\_JunD\_Veh\_GJF\_16-07-23-2,23312576,18219803  
 C57Bl6\_Thiomac\_ChIP\_PPARG\_Veh\_NJS\_13-04-03-1,21860144,15126901  
 C57Bl6\_Thiomac\_ChIP\_PPARG\_Veh\_NJS\_13-04-03-2,18484526,13443728  
 C57Bl6-JunKO-Atf3DBD\_iBMDM\_ChIP\_Veh\_GJF\_18-02-20-rep1,12013556,8365475  
 C57Bl6-JunKO-Atf3DBD\_iBMDM\_ChIP\_Veh\_GJF\_18-02-20-rep2,20769247,15335656

## Antibodies

Fos Rabbit polyclonal Santa Cruz sc-7202  
 FosL1 Rabbit polyclonal Santa Cruz sc-605  
 FosL2 Mouse monoclonal Santa Cruz sc-166102  
 Fosb Rabbit polyclonal Cell Signaling 2251  
 Jun Rabbit polyclonal Santa Cruz sc-1694  
 Jun Mouse monoclonal Santa Cruz sc-74543  
 JunB Rabbit polyclonal Santa Cruz sc-73  
 JunD Rabbit polyclonal Santa Cruz sc-74  
 Jdp2 Rabbit polyclonal Thermo PA5-19692  
 Batf Rabbit polyclonal Brookwood Biomedical PAB4003  
 Batf2 Rabbit polyclonal Santa Cruz sc-241891  
 Batf3 Rabbit polyclonal Abnova H00055509-M04  
 C/ebp Rabbit polyclonal Santa Cruz sc-61  
 Pu.1 Rabbit polyclonal Santa Cruz sc-352  
 PPARG Rabbit polyclonal Santa Cruz sc-7196  
 PPARG Rabbit monoclonal Cell Signaling C26H12  
 PPARG Rabbit polyclonal Diagenode C15410133

## Peak calling parameters

eads from each ChIP-seq sample were aligned to the mm10 build of the mouse genome using bowtie2 (with default parameters).  
 Sam files were converted to tag directories with HOMER  
 Peaks were called with HOMER with the findPeaks command using the corresponding input file and the parameters -L 0 -C 0 -fdr 0.9  
 HOMER peak scores from peak files corresponding to replicate experiments were used as input for IDR; peaks with IDR < 0.05 were retained  
 Genome\_build: mm10  
 Supplementary\_files\_format\_and\_content: tab delimited file giving the genomic coordinates of putative binding site for each ChIP target. The "count" column indicates the HOMER peak score

## Data quality

Peaks were filtered out by calculating the Irreproducible Discovery Rate (using the HOMER peak score as input for IDR). We filtered away all peaks that had IDR  $\geq$  0.05.

## Software

HOMER was used to perform peak calling (<http://homer.ucsd.edu/homer/>)

The IDR program was used to calculate IDR scores (<https://github.com/nboley/idr>)