

# Supplementary Note 2

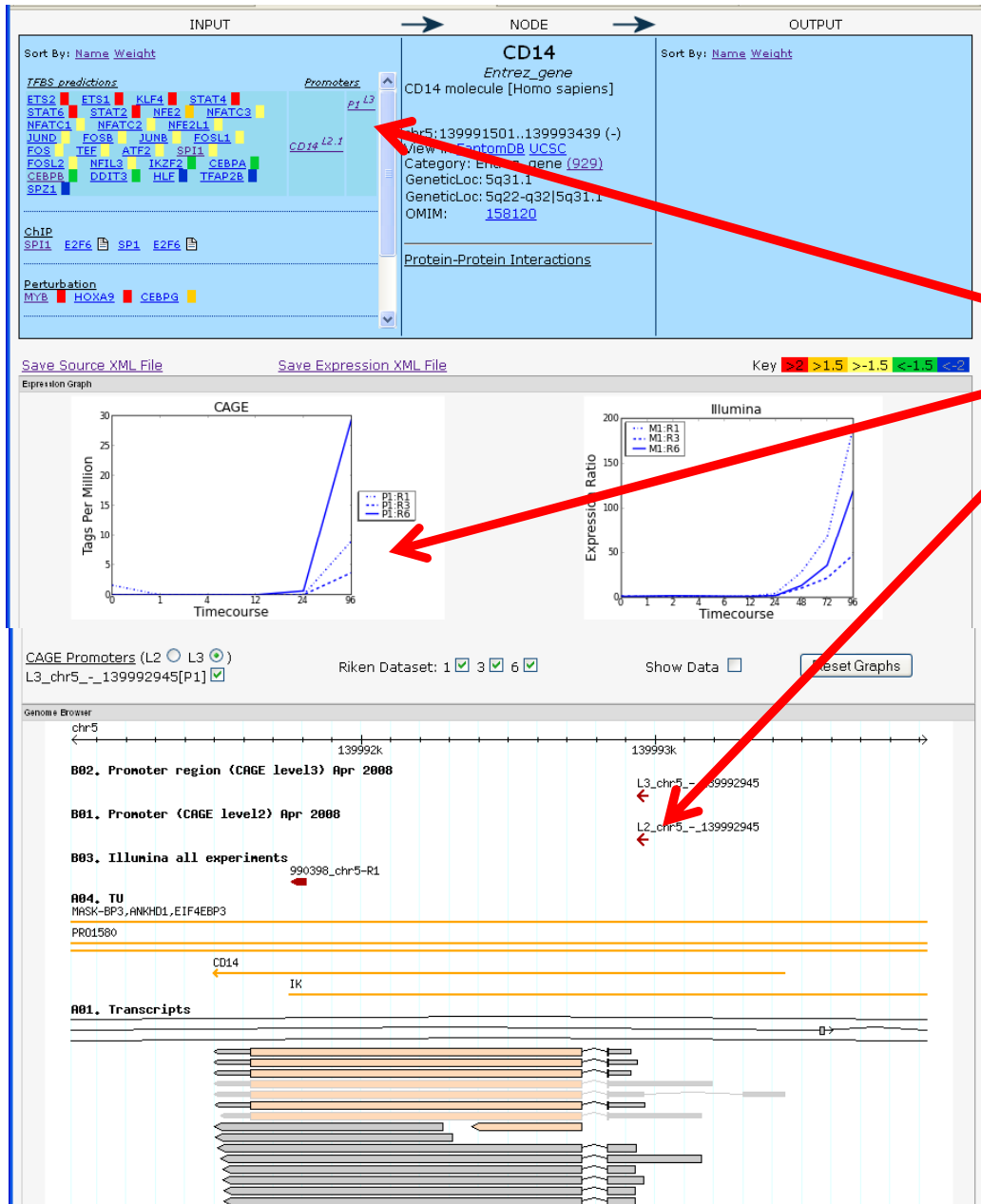
This supplementary note provides example views for the key monocytic marker CD14. The examples covers the gene centric and subnetwork views. The various edge types and expresison data, and how to extract the transcription factor binding site predictions from the genome browser.

Sections:

1. CAGE promoters
2. TFBS predictions
3. ChIP edges
4. Perturbation edges (siRNA against TF and miRNA overexpression)
5. Summary of inputs using sub-network view

# 1. CAGE promoters:

CAGE promoters are presented in 3 places within the EEDB gene centric view



- CD14 promoter(L3\_chr5 - 139992945)
- TFBS predictions (top left)
- Expression (middle left)
- Genomic location (bottom)

# 1. CAGE promoters:

Popup explaining CAGE defined promoters

The screenshot shows the FANTOM4 GNP-ECW website interface. At the top, there are navigation tabs: Home, Genome Browser, EdgeExpressDB, Data, and Paper. Below these are links for FANTOM4 EdgeExpressDB, about, center view, subnet view, and contents. A search bar contains 'cd14', and below it are links for ACE, BSG, CD14, CDH5, F3, MCAM, NDUFA2, PDGFRA, PDGFRB, PTPRJ, and THBD. A flow diagram shows INPUT (TFBS predictions) leading to a central NODE (CD14) and then to OUTPUT (TFBS predictions). The CD14 node is expanded to show 'Entrez\_gene' and 'CD14 molecule [Homo sapiens]'. A popup window titled 'CAGE DEFINED PROMOTERS' is overlaid on the page, providing detailed information about promoter levels and CAGE regions. The popup text is as follows:

**CAGE DEFINED PROMOTERS**

**PROMOTER LEVELS:** For FANTOM4 we developed three levels to describe the relationship between individual transcription start sites (TSS), promoters and promoter regions. Individual TSS are referred to as level 1 (L1), nearby TSSs positions whose expression profiles are the same up to measurement noise are clustered into promoters (L2) and adjacent promoters that are within 400bp of each other are condensed into 'promoter regions' (L3). For further details on promoter levels please refer to the FANTOM4 main manuscript (Suzuki et al. 2009).

P1<sup>L3</sup> corresponds to a level 3 promoter region of a gene which can contain multiple level 2 promoters (eg. Gene<sup>L2,1</sup> and Gene<sup>L2,2</sup>). Note: TFBS predictions are done per level3, BUT response weight is calculated for each level 2 promoter

Upon mouse-over the promoter ID [of the form L3\_chr21\_+\_39099722] will be displayed. If the user clicks on this, it will open a genome browser page focused on the promoter region (-300 +100), displaying the promoters and the TFBS predicted in that region. This can be used to extract individual sites for CHIP and EMSA validation experiments.

At the bottom of the popup, there is a key: >2 (red), >1.5 (yellow), >-1.5 (green), <-1.5 (blue), <-2 (dark blue).

Below the popup, there is a 'Save Source XML File' link and an 'Expression Graph' section showing a CAGE region (30) and an Illumina region (200).

# 1. CAGE promoters:

For CD14, deepCAGE on THP-1 identifies one L3 promoter region (L3\_chr5\_-\_139992945). TFBS predictions are carried out in the for a window of -300 to +100bp of each L3.

**FANTOM4 GNP-ECW** RIKEN RIKEN OSC

Home | Genome Browser | **EdgeExpressDB** | Data | Paper

FANTOM4 EdgeExpressDB | about | center view | subnet view | contents

Search:  [ACE](#) [BSG](#) [CD14](#) [CDH5](#) [F3](#) [MCAM](#) [NDUFA2](#) [PDGFRA](#) [PDGFRB](#) [PTPRJ](#) [THBD](#)

(Display Ensembl ids)

INPUT → NODE → OUTPUT

**CD14**  
Entrez\_gene  
CD14 molecule [Homo sapiens]

**L3\_chr5\_-\_139992945** L3 promoter :  
CAGE\_L3\_promoter\_april2008  
location: :: chr5:139992942..139992976-  
maxexpress: CAGE:29.32

Sort By: [Name](#) [Weight](#)

TFBS predictions

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUN	FOSB	JUN	
FOS	TEF	ATF2	
FOSL2	NFIL3	IK	
CEBPB	DDIT3	H	
SPZ1			

Promoters

ChIP  
[SPI1](#) [E2F6](#) [SP1](#) [E2F6](#)

Perturbation  
[MYB](#) [HOXA9](#) [CEBPG](#)

OMIM: [158120](#)

Protein-Protein Interactions

Sort By: [Name](#) [Weight](#)

[Save Source XML File](#) [Save Expression XML File](#) Key >2 >1.5 >-1.5 <-1.5 <-2

Expression Graph

30 CAGE 200 Illumina

# 1. CAGE promoters:

The L3 promoter region (L3\_chr5\_-\_139992945) contains one L2 promoter (L2\_chr5\_-\_139992945).

INPUT → NODE → OUTPUT

**INPUT**

Sort By: [Name](#) [Weight](#)

*TFBS predictions*

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUND	FOSB	JUNB	FOSL1
FOS	TEF	ATF2	SPI1
FOSL2	NFIL3	IKZF2	CEBPA
CEBPB	DDIT3		
SPZ1			

*Promoters*

[p1 L3](#)

[CD14 L2.1](#)

**L2\_chr5\_-\_139992945** L2\_promoter  
CAGE\_L2\_promoter\_april2008

location: chr5:139992942..139992976-  
maxexpress: CAGE:29.32

*ChIP*

[SPI1](#) [E2F6](#)

*Perturbation*

[MYB](#) [HOXA9](#) [CEBPG](#)

**NODE**

**CD14**  
*Entrez\_gene*  
CD14 molecule [Homo sapiens]

chr5:139991501..139993439 (-)  
View in [FantomDB](#) [UCSC](#)  
Category: Entrez\_gene (929)  
Chromosomal Location: 5q31.1  
Chromosomal Location: 5q22-q32|5q31.1  
RefSeq ID: [158120](#)

*Protein-Protein Interactions*

**OUTPUT**

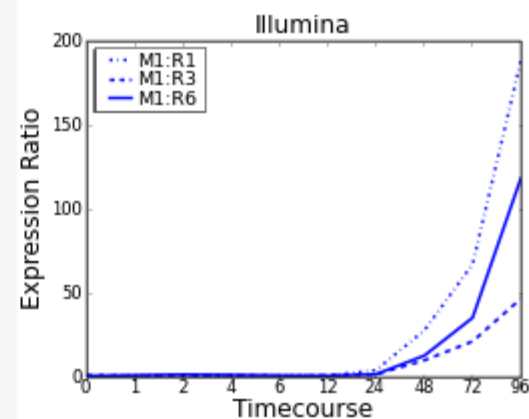
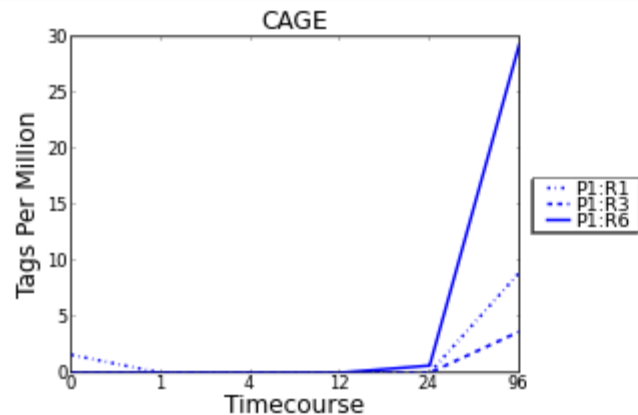
Sort By: [Name](#) [Weight](#)

[Save Source XML File](#)

[Save Expression XML File](#)

Key >2 >1.5 >-1.5 <-1.5 <-2

Expression Graph



## 2. TFBS predictions

Popup explaining TFBS predictions and edge weights in EEDB. For each L2 promoter, response Weights are calculated that reflect how well the expression pattern of the L2, matches the

The screenshot displays the FANTOM4 GNP-ECW EdgeExpressDB interface. At the top, there are navigation tabs for Home, Genome Browser, EdgeExpressDB (selected), Data, and Paper. Below the tabs, there are links for FANTOM4 EdgeExpressDB, about, center view, subnet view, and contents. A search bar contains 'cd14', and a list of related genes is shown: ACE, BSG, CD14, CDH5, F3, MCAM, NDUFA2, PDGFRA, PDGFRB, PTPRJ, THBD. A diagram shows the flow from INPUT to NODE to OUTPUT. The INPUT section shows TFBS predictions for CD14, with a red arrow pointing to a popup. The NODE section shows CD14 details, including Entrez\_gene (929) and coordinates. The OUTPUT section is empty. A key at the bottom right shows response weight ranges: >2 (red), >1.5 (orange), >-1.5 (yellow), <-1.5 (green), <-2 (blue). The bottom of the page shows an Expression Graph with CAGE and Illumina tracks.

**FANTOM4 GNP-ECW**

Home Genome Browser **EdgeExpressDB** Data Paper

FANTOM4 EdgeExpressDB about center view subnet view contents

Search:  [ACE](#) [BSG](#) [CD14](#) [CDH5](#) [F3](#) [MCAM](#) [NDUFA2](#) [PDGFRA](#) [PDGFRB](#) [PTPRJ](#) [THBD](#)

(Display Ensembl ids)

INPUT → NODE → OUTPUT

Sort By: [Name](#) [Weight](#)

**TFBS predictions**

**TFBS EDGES:** Evolutionarily conserved Transcription factor binding sites are predicted using MOTEVO with a set of non-redundant matrices (combining JASPAR, TRANSFAC and a small set of de-novo motifs trained on ChIP-chip datasets).

**TFBS WEIGHTS:** The weights on TFBS edges are 'response values', these are central to the FANTOM4 analysis and basically say how well the expression of each LEVEL2 promoter responds to (or matches) the motif activity for that factor (eg. MYB motif activity decreases as the cells differentiate and PRTN3 a known (and predicted) target of MYB is down-regulated, hence it has a high response weight of 14.125). We recommend to users wishing to validate sites, response weights >1.5 are more reliable. For more detail on TFBS prediction and motif activity please refer to the FANTOM4 manuscript (Suzuki et al. 2009).

**CD14**  
Entrez\_gene  
CD14 molecule [Homo sapiens]

991501..139993439 (-)  
[FANTOM4](#) [UCSC](#)  
Entrez\_gene ([929](#))  
Chromosome: 5q31.1  
Coordinates: 5q22-q32|5q31.1  
[158120](#)

[Protein Interactions](#)

Save Source XML File Save Expression XML File

Key ■ >2 ■ >1.5 ■ >-1.5 ■ <-1.5 ■ <-2

Expression Graph

30 CAGE 200 Illumina

## 2. TFBS predictions

Popup on ETS2 – predicted regulator of CD14, weight>1.5 is high probability

**FANTOM4 GNP-ECW** RIKEN RIKEN OSC

Home | **Genome Browser** | EdgeExpressDB | Data | Paper

FANTOM4 EdgeExpressDB | about | center view | subnet view | contents

Search:  [ACE](#) [BSG](#) [CD14](#) [CDH5](#) [F3](#) [MCAM](#) [NDUFA2](#) [PDGFRA](#) [PDGFRB](#) [PTPRJ](#) [THBD](#)

(Display Ensembl ids)

INPUT → NODE → OUTPUT

**INPUT**

Sort By: [Name](#) [Weight](#)

TFBS predictions

ETS2 ■ ETS1 ■ KLF4 ■ STAT4 ■  
STAT6 ■ STAT2 ■ NFE2 ■ NFATC3 ■

**ETS2** popup:  
Name: ETS2  
Id: 5557730  
Source: Entrez\_TFBS\_promoter\_may08  
Weight: 3.985  
Evidence: Predicted  
Matrix: EVN33

Promoters

CD14<sup>L2.1</sup> P1 L3

**ChIP**  
[SPI1](#) [E2F6](#) [SP1](#) [E2F6](#)

**Perturbation**  
[MYB](#) ■ [HOXA9](#) ■ [CEBPG](#) ■

**NODE**

**CD14**  
*Entrez\_gene*  
CD14 molecule [Homo sapiens]

chr5:139991501..139993439 (-)  
View in [FantomDB](#) [UCSC](#)  
Category: Entrez\_gene ([929](#))  
GeneticLoc: 5q31.1  
GeneticLoc: 5q22-q32|5q31.1  
OMIM: [158120](#)

Protein-Protein Interactions

**OUTPUT**

Sort By: [Name](#) [Weight](#)

[Save Source XML File](#) [Save Expression XML File](#) Key >2 >1.5 >-1.5 <-1.5 <-2

Expression Graph

30 CAGE 200 Illumina

## 2. TFBS predictions

Clicking on either the L2 or L3 promoter will launch a genome browser window focused on the L3 promoter region showing the predicted transcription factor binding sites

INPUT → NODE → OUTPUT

Sort By: [Name](#) [Weight](#)

**TFBS predictions**

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUND	FOSB	JUNB	FOSL1
FOS	TEF	ATF2	SPI1
FOSL2	NFIL3	IKZF2	CEBPA
CEBPB	DDIT3		
SPZ1			

**Promoters**

*p1* *L3*

*CD14 L2.1*

**L2\_chromosome\_5\_-\_139992945 L2\_promoter**  
CAGE\_L2\_promoter\_april2008  
location: :: chr5:139992942..139992976-  
maxexpress: CAGE:29.32

**CD14**  
*Entrez\_gene*  
CD14 molecule [Homo sapiens]  
chr5:139991501..139993439 (-)  
View in [FantomDB](#) [UCSC](#)  
Category: Entrez\_gene (929)  
transcriptLoc: 5q31.1  
transcriptLoc: 5q22-q32|5q31.1  
transcriptStart: [158120](#)

**ChIP**  
[SPI1](#) [E2F6](#)

**Perturbation**  
[MYB](#) [HOXA9](#) [CEBPG](#)

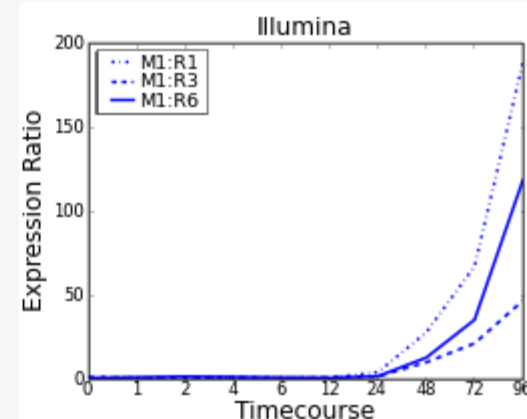
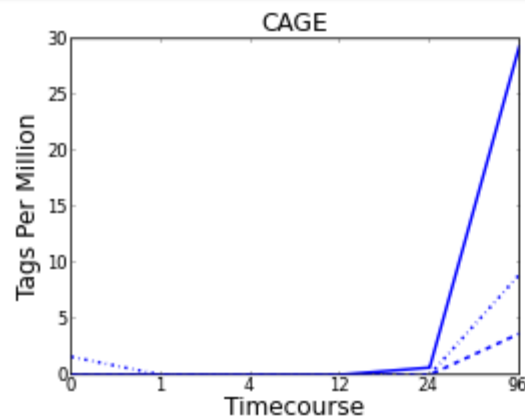
**Protein-Protein Interactions**

[Save Source XML File](#)

[Save Expression XML File](#)

Key >2 >1.5 >-1.5 <-1.5 <-2

Expression Graph





## 2. TFBS predictions

The window is focused on the -300, +100 bp region used for the TFBS predictions.

The screenshot displays the FANTOM4 GNP-ECW genome browser interface. The main content area shows the 'Human (hg18) genome viewer for THP-1 analysis [Release 2008/09/05]' with a focus on 435 bp from chromosome 5, positions 139,992,842 to 139,993,276. The 'Details' section is expanded to show 'TFBS HotEvo cage' predictions. A large red arrow points from the 'TFBS HotEvo cage' section to the 'TF\_binding\_site\_cage\_030708:NFATC-20291 Details' panel on the right.

**TFBS HotEvo cage**

TFBS	posterior_prob
NFATC-20291	0.95
PU_1-218716	0.92
NFE2-3124	0.63
ZNF1142-92660	0.99
STAT2_4,6-13206	0.86
HLF4-13683	0.85
STAT2_4,6-13207	0.80
HLF-142765	0.99
ETS1_2-23236	0.94
ATF2-4173	0.98
NFE2L1-182380	0.32
CEBPA_8_001T3-117685	0.76
FOS.B.L1_L1_UNB_0-187311	0.63
NFIL3-119885	1.00
FOSL2-87934	0.63
TEF-71565	0.73
TFAP2B-81409	0.59
SPZ1-190766	0.35
PU_1-218717	0.97
HLF4-136832	0.96

### TF\_binding\_site\_cage\_030708:NFATC-20291 Details

**Name:** NFATC-20291  
**Class:** TF\_binding\_site\_cage\_030708  
**Type:** TF\_binding\_site\_cage\_030708  
**Source:** MOTEVOC  
**Position:** chr5:139992897..139992908 (- strand)  
**Length:** 12  
**Score:** 0.950002  
**L2\_DATA:** L2\_chr5\_-139992945:0.950002218458349:L1\_chr5\_-139992942:39  
**L3\_ID:** L3\_chr5\_-139992945

```
>NFATC-20291 class=TF_binding_site_cage_030708 position=chr5:139992897..139992908 (- strand)
TGTAGGAAAG AA
```

Clicking on the TFBS predictions themselves will then allow the user to get the co-ordinates Of the predicted site

### 3. CHIP edges

Popup explaining chromatin immunoprecipitation edges

INPUT → NODE → OUTPUT

Sort By: [Name](#) [Weight](#)

*TFBS predictions*

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUND	FOSB	JUNB	FOSL1
FOS	TEF	ATF2	SPI1
FOSL2	NFIL3	IKZF2	CEBPA
CEBPB	DDIT3	HLF	TFAP2B
SPZ1			

*Promoters*

*CD14* L2.1

*CD14* L3

**CD14**  
*Entrez\_gene*  
CD14 molecule [Homo sapiens]

chr5:139991501..139993439 (-)  
View in [FantomDB](#) [UCSC](#)  
Category: Entrez\_gene (929)  
GeneticLoc: 5q31.1  
GeneticLoc: 5q22-q32|5q31.1  
OMIM: [158120](#)

Sort By: [Name](#) [Weight](#)

ChIP  
[SPI1](#) [E2F6](#) [SP1](#) [E2F6](#)

**ChIP**

**ChIP EDGES:** The FANTOM4 consortium generated chromatin immunoprecipitation on chip data for SPI1 and SP1, for these factors, a peak of binding within 1kb of a promoter is considered positive evidence for an edge between these factors and the target gene. Public ChIP-chip and ChIP-seq datasets were also incorporated, for these we relied on the primary publication's definition of positive binding, and we include a PubMed link back to the corresponding citation.

**ChIP WEIGHTS:** The weights used here are the number of experiments this TF has been observed binding at the target gene's promoter (ie. a weight of 4, means it has been observed in 4 separate ChIP-chip experiments).

Key >2 >1.5 >-1.5 <-1.5 <-2

**Tags Per Million**

Timecourse	SPI1:R1	SPI1:R3	SPI1:R6
0	~1	~1	~1
1	~0.5	~0.5	~0.5
4	~0.2	~0.2	~0.2
12	~0.1	~0.1	~0.1
24	~0.5	~0.5	~0.5
96	~8	~4	~22

**Expression Ratio**

Timecourse	M1:R1	M1:R3	M1:R6
0	~0	~0	~0
1	~0	~0	~0
2	~0	~0	~0
4	~0	~0	~0
6	~0	~0	~0
12	~0	~0	~0
24	~10	~5	~5
48	~40	~20	~15
72	~100	~50	~40
96	~180	~100	~80

### 3. CHIP edges

Popup for E2F6, weight is 2, as binding was observed in 2 separate chip experiments.

Note: clicking on the manuscript icon will take the user to the pubmed article

FANTOM4 EdgeExpressDB [about](#) [center view](#) [subnet view](#) [contents](#)

Search:

(Display Ensembl ids)

INPUT → NODE → OUTPUT

Sort By: [Name](#) [Weight](#)

*TFBS predictions*

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUND	FOSB	JUNB	FOSL1
FOS	TEF	ATF2	SPI1
FOSL2	NFIL3	IKZF2	CEBPA
CEBPB	DDIT3	HLF	TFAP2B
SPZ1			

*Promoters*

*p1 L3*

*CD14 L2.1*

**ChIP**

[SPI1](#) [E2F6](#) [SP1](#) [E2F6](#)

**Perturb**

[MYB](#)

**CD14**  
*Entrez\_gene*  
CD14 molecule [Homo sapiens]  
chr5:139991501..139993439 (-)  
View in [FantomDB](#) [UCSC](#)  
Category: Entrez\_gene ([929](#))  
GeneticLoc: 5q31.1  
GeneticLoc: 5q22-q32|5q31.1  
OMIM: [158120](#)

Protein-Protein Interactions

Name: E2F6  
Id: 5542588  
Source: CHIP\_chip  
Weight: 2.000

[Save Source XML File](#) [Save Expression XML File](#) Key  >2   >1.5   >-1.5   <-1.5   <-2

Expression Graph

**CAGE**

**Illumina**

### 3. Perturbation edges (siRNA against TF and miRNA overexpression)

Popup explaining perturbation edges

INPUT
→
NODE
→
OUTPUT

Sort By: [Name](#) [Weight](#)

*TFBS predictions*

ETS2	ETS1	KLF4	STAT4
STAT6	STAT2	NFE2	NFATC3
NFATC1	NFATC2	NFE2L1	
JUND	FOSB	JUNB	FOSL1
FOS	TEF	ATF2	SPI1
FOSL2	NFIL3	IKZF2	CEBPA
CEBPB	DDIT3	HLF	TFAP2B
SPZ1			

*Promoters*

*CD14<sup>L2.1</sup>*

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*ChIP*

[SPI1](#) [E2F6](#) [SP1](#) [E2F6](#)

---

*Perturbation*

[MYB](#) [HES1](#) [CEBPG](#)

**CD14**

*Entrez\_gene*

CD14 molecule [Homo sapiens]

chr5:139991501..139993439 (-)

View in [FantomDB](#) [UCSC](#)

Category: Entrez\_gene ([929](#))

GeneticLoc: 5q31.1

GeneticLoc: 5q22-q32|5q31.1

OMIM: [158120](#)

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[Protein-Protein Interactions](#)

Sort By: [Name](#) [Weight](#)

**Perturbation**

**PERTURBATION EDGES:** siRNA knockdown(KD) of 52 transcription factors(TF) and over-expression of 12 miRNAs was used to identify TFs and miRNAs involved in THP-1 differentiation and maintenance of the undifferentiated state. Affected genes were assessed by Illumina microarrays 48 hours post transfection. The array data was quantile normalized and compared to negative control siRNAs and pre-miRNAs to identify genes that are specifically perturbed in response to the TF/miRNA.

**PERTURBATION WEIGHTS:** The perturbation edges displayed in EEDB are stringently filtered, by log fold change  $\geq 1 / \leq -1$  and B-statistic  $\geq 2.5$ . A positive log FC means the transcript is induced upon knockdown of the siRNA or over-expression of the miRNA. A negative log FC means the transcript is down-regulated in response to the perturbation (eg. CD14 is strongly induced upon MYB KD and has a log FC of 6.8, whereas vitrin is strongly repressed upon MYB KD and has a log FC of -4.0).

>2
>1.5
>-1.5
<-1.5
<-2

Tags Per Million

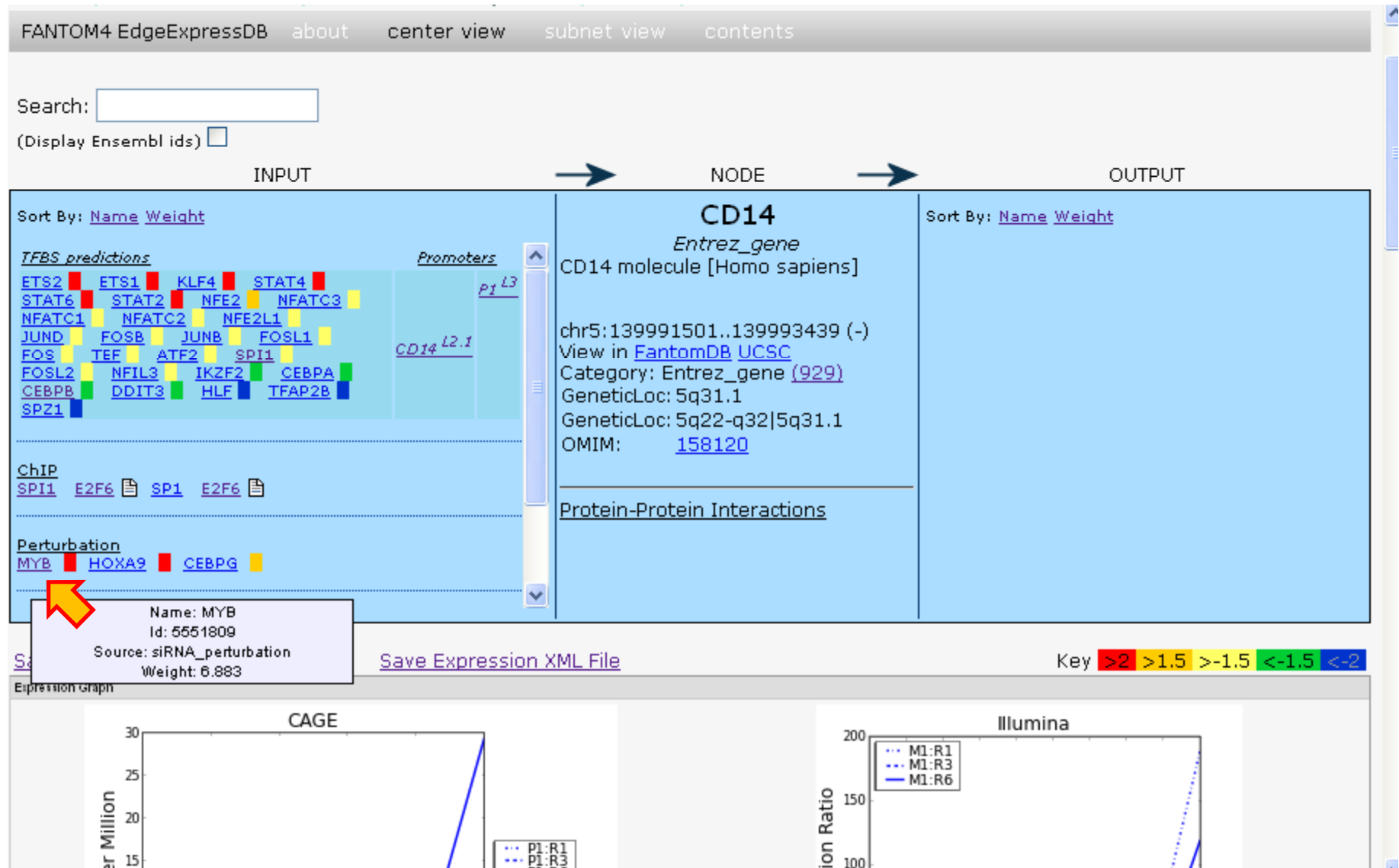
Timecourse

Expression Ra

Timecourse

### 3. Perturbation edges (siRNA against TF and miRNA overexpression)

siRNA KD of MYB, HOXA9 and CEBPG induces CD14 expression in THP-1 cells as detected By Illumina microarray



### 3. Summary of regulatory inputs into CD14

Pop-up tooltip explaining the interface and the legend

The screenshot shows the FANTOM4 GNP-ECW website interface. At the top, there are navigation tabs: Home, Genome Browser, EdgeExpressDB (selected), Data, and Paper. Below the tabs is a search bar with the text "prefix search:" and a text input field. To the right of the search bar is a link "EEDB subnet LEGEND info" with a red arrow pointing to it. The main content area is a pop-up tooltip titled "THE SUBNET VIEW" in red. The tooltip contains the following text:

**THE SUBNET VIEW**  
The subnet view allows for one to input a list of gene and/or miRNA names as nodes in a graph. The system will search for all matching connecting edges within that set of nodes based on user selectable edge filters.

**INTERFACE:**  
**NODE SELECTION:** Users enter Entrez genes and mirbase microRNA IDs into the text box  
**PRIMARY EDGE TYPES:** The system allows for simple logic by providing two edge sets (primary and secondary). If only edges in set1 are selected then a simple search is performed.  
**SECONDARY EDGE TYPES:** If edges from both sets are selected the search is performed for genes that are connected by BOTH lines of evidence (eg. TFBS prediction in set 1 and perturbation or CHIP in set2), this can be used to prune TFBS predictions to only those for which there is some experimental support.  
**HIDE SINGLETONS:** Hides nodes that have no incoming or outgoing edges (default is on)  
**HIDE LEAVES:** Hides nodes with only incoming edges (default is off)

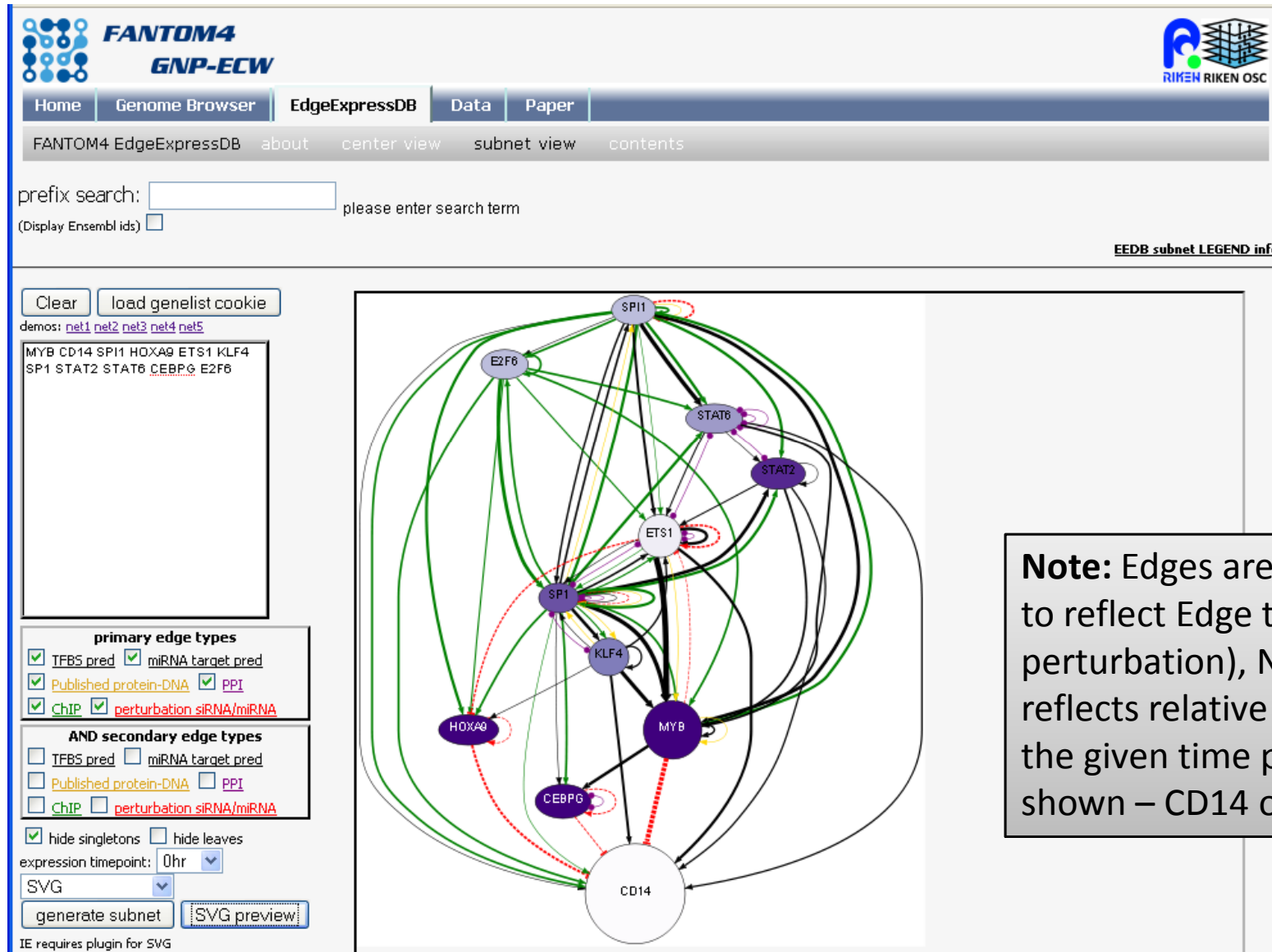
**LEGEND:**  
**EDGE COLOURS:** BLACK-- FANTOM4 Transcription factor binding site predictions and miRNA target predictions, YELLOW-- published protein-DNA edges, PURPLE-- protein-protein interactions, GREEN-- chip-chip(protein-DNA) edges, RED-- siRNA and miRNA perturbation edges.  
**EDGE LINE STYLE:** SOLID-- Direct edges, DASHED-- perturbation edges (possibly direct or indirect)  
**EDGE TERMINATORS:** Arrowhead-- activating relationships, Blunt-- repressing relationships, Round-- bidirectional protein-protein relationships  
**NODE SHAPE:** Round nodes are genes, hexagonal nodes are miRNAs.  
**NODE DIAMETER:** The diameter of each node is scaled to indicate the 'dynamics' of the gene. Calculated by mapping to  $\log(\max(\text{detected ILMN expression})/\min(\text{detected ILMN expression}))$  within the time course. Highly dynamic nodes are larger than statically expressed nodes.  
**NODE COLOUR:** The color of the node is mapped to a relative scale for each node between white for  $\min(\text{detected ILMN expression})$  and purple  $\max(\text{detected ILMN expression})$ . If the node has no detectable ILMN expression, the name of the node becomes red and the background is white.

The tooltip also includes a list of gene names: MYB CD14 SP11 HOXA9 ETS1 SP1 STAT2 STAT6 CEBPG E2. Below the list are checkboxes for "primary edge types" (TFBS pred, miRNA target, Published protein-DNA, ChIP, perturbation siRNA/miRNA) and "AND secondary edge types" (TFBS pred, miRNA target pred, Published protein-DNA, PPI, ChIP, perturbation siRNA/miRNA). There are also checkboxes for "hide singletons" and "hide leaves", and a dropdown menu for "expression timepoint" set to "96hr". At the bottom of the tooltip are buttons for "generate subnet" and "SVG preview".

Below the tooltip is a network diagram showing a central purple node labeled "CD14". It is connected to several other nodes: HOXA9 (grey), MYB (grey), CEBPG (grey), and ETS1 (grey). The connections are represented by various colored and styled lines: a solid black line from MYB to CD14, a solid black line from HOXA9 to CD14, a solid black line from CEBPG to CD14, a solid black line from ETS1 to CD14, a dashed red line from MYB to CD14, a dashed red line from HOXA9 to CD14, a dashed red line from CEBPG to CD14, a dashed red line from ETS1 to CD14, a solid green line from HOXA9 to CD14, a solid green line from MYB to CD14, a solid green line from CEBPG to CD14, and a solid green line from ETS1 to CD14. There are also bidirectional connections between HOXA9 and MYB, and between CEBPG and ETS1, represented by solid black lines with rounded terminators.

### 3. Summary of regulatory inputs into CD14

Sub-network view of CD14 with selected upstream regulators



### 3. Summary of regulatory inputs into CD14

Same sub-network view of CD14 but with 96h expression data (note CD14 is induced – purple)

