Tyrant Cistrome – Identifying the set of transcription factors 'ruling' the expression of a gene

Problem:

The ENCODE (Encyclopedia of DNA Elements) Consortium resulted in a comprehensive list of transcription factor ChIP-Seq data, proving to be a treasure trove of information about how a gene might be transcriptionally regulated.

However, binding sites identified by ChIP-Seq are not only found in the promoter regions of a gene but also in distal intergenic region or introns.

Most TF binding appears to be promiscuous, with low occupancy and non-functional, whereas functional TF binding is characterized by high occupancy. In practice, binding locations of functionally diverse TFs overlap substantially with each other and regions of open chromatin.

How to distinguish between functional and non-functional TF binding?


RefSeq Genes
CDH3
CDH1
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs
Which TFs are most likely to regulate your gene?
How to prioritize?

Regulatory potential – the gene's likelyhood of being regulated by a transcription factor

k: the number of binding sites within 100 kb of gene g

$$S_g = \sum_{i=1}^{k} e^{-(0.5+4\Delta_i)},$$

Δi: the distance between site i and the TSS of gene g normalized to 100 kb (e.g., 0.5 for a 50-kb distance).

Features:

1. The influence of each binding site on gene regulation is modeled as a function that decreases monotonically with increasing distance from the TSS.

2. The shape of this function approximates empirical observations of the distance between binding sites and differentially expressed genes in multiple ChIP-seq experiments.

3. The constant in the equation enables the exponential function to adopt more flexible shapes and 0.5 was derived to better fit ChIA-PET and Hi-C data.

Tang, Q. et al. A comprehensive view of nuclear receptor cancer cistromes. Cancer Res. 71, 6940–6947 (2011).

Tyrant Cistrome – Identifying the set of transcription factors 'ruling' the expression of a gene

How:

$$S_g = \sum_{i=1}^{k} e^{-(0.5+4\Delta_i)},$$

We calculated for each of the 161 transcription factors contained in the ENCODE TFBS ChIP-Seq data sets, their regulatory potential on each of the 25,635 genes annotated in the human hg19 genome assembly.

Tyrant Cistrome allows you:

1. To identify the transcription factors having the highest regulatory potential for your gene of interest.

2. To visualize the associated ChIP-Seq peak regions for these regulatory transcription factors together with the integrated regulation from ENCODE tracks of UCSC genome (http://genome-euro.ucsc.edu/index.html) to get a useful insight in the different aspects of how your gene might be regulated.

3. To get a sorted list of genes that share a considerable fraction of the regulatory transcription factors of your gene of interest.

https://bioit2.irc.ugent.be/intra/tyrant/ (login required)

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier gene id

Select P-value cutoff 0.05

Select similarly regulated Jaccard distance cutoff 0.50

Reset Filter

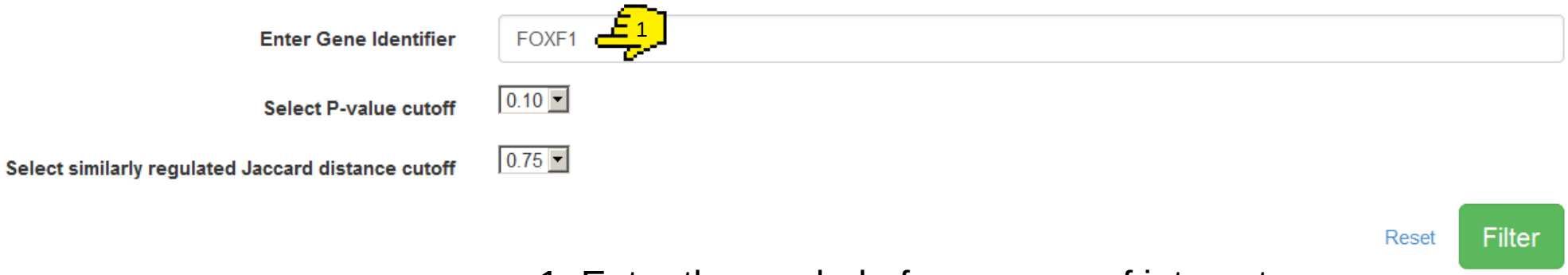
Rationale

A cistrome can be defined as a set of cis-acting elements bound by a trans-acting factor (aka transcription factor) at the genomic scale. Cistromes as such correspond to binding sites identified by ChIP-Seq experiments (Tang et al, http://cancerres.aacrjournals.org/content/71/22/6940 A major challenge is to link cistromes (or binding sites of a transcription factor) with direct target genes of that factor. However, binding sites identified by ChIP-Seq are not only found in the promoter regions of a gene but also in distal intergenic region or introns. They may contribute to regulation of gene expression through long-distance chromatin interactions. These long-distance chromatin interactions are typically studied by Hi-C, a method that probes the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing (Lieberman-Aiden et al, http://www.sciencemag.org/content/326/5950/289), and ChIA-PET, a combination of the existing methods of chromatin immunoprecipitation (ChIP) and paired-end ditag (PET) sequencing (Fullwood et al, http://www.nature.com/nature/journal /v462/n7269/full/nature08497.html). While these methods are not able to link a transcription factor binding site to its target gene, they clearly showed that interactions within single chromosomal arms exhibit in a predictable way a decrease of the contact probability P with genomic distances (Dekker et al, http://www.nature.com/nrg/journal/v14/n6/full/nrg3454.html).

Based on the findings that (1) enhancer regulation potential is proportional to the number of binding sites near a gene and (2) that the trend of chromatin interactions diminishes in a predictable way with increasing genomic distance, Tang et al (http://cancerres.aacrjournals.org/content/71/22/6940) proposed to calculate the regulatory potential of a transcription factor for a given gene as the sum of the nearby binding sites weighted by the distance from each site to the transcription start site (TSS) of the gene.

We have adapted this method and calculated for each of the 161 transcription factors contained in the ENCODE TFBS ChIP-Seq data sets, their regulatory potential on each of the 25635 genes annotated in the human hg19 genome assembly. Tyrant Cistrome allows you (1) to identify the transcription factors having the highest regulatory potential for your gene of interest, (2) to visualize the associated ChIP-Seq peak regions for these regulatory transcription factors together with the integrated regulation from ENCODE tracks of UCSC genome (http://genome-euro.ucsc.edu/index.html) to get a useful insight in the different aspects of how your gene might be regulated and (3) to get a sorted list of genes that share a considerable fraction of the regulatory transcription factors of your gene of interest.

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene



1. Enter the symbol of your gene of interest

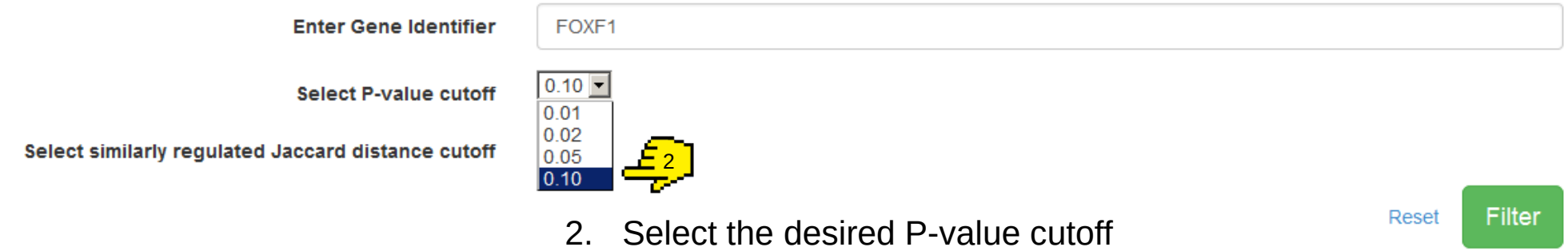
Rationale

A cistrome can be defined as a set of cis-acting elements bound by a trans-acting factor (aka transcription factor) at the genomic scale. Cistromes as such correspond to binding sites identified by ChIP-Seq experiments (Tang et al, http://cancerres.aacrjournals.org/content/71/22/6940 A major challenge is to link cistromes (or binding sites of a transcription factor) with direct target genes of that factor. However, binding sites identified by ChIP-Seq are not only found in the promoter regions of a gene but also in distal intergenic region or introns. They may contribute to regulation of gene expression through long-distance chromatin interactions. These long-distance chromatin interactions are typically studied by Hi-C, a method that probes the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing (Lieberman-Aiden et al, http://www.sciencemag.org/content/326/5950/289), and ChIA-PET, a combination of the existing methods of chromatin immunoprecipitation (ChIP) and paired-end ditag (PET) sequencing (Fullwood et al, http://www.nature.com/nature/journal/v462/n7269/full/nature08497.html). While these methods are not able to link a transcription factor binding site to its target gene, they clearly showed that interactions within single chromosomal arms exhibit in a predictable way a decrease of the contact probability P with genomic distances (Dekker et al, http://www.nature.com/nrg/journal/v14/n6/full/nrg3454.html).

Based on the findings that (1) enhancer regulation potential is proportional to the number of binding sites near a gene and (2) that the trend of chromatin interactions diminishes in a predictable way with increasing genomic distance, Tang et al (http://cancerres.aacrjournals.org/content/71/22/6940) proposed to calculate the regulatory potential of a transcription factor for a given gene as the sum of the nearby binding sites weighted by the distance from each site to the transcription start site (TSS) of the gene.

We have adapted this method and calculated for each of the 161 transcription factors contained in the ENCODE TFBS ChIP-Seq data sets, their regulatory potential on each of the 25635 genes annotated in the human hg19 genome assembly. Tyrant Cistrome allows you (1) to identify the transcription factors having the highest regulatory potential for your gene of interest, (2) to visualize the associated ChIP-Seq peak regions for these regulatory transcription factors together with the integrated regulation from ENCODE tracks of UCSC genome (http://genome-euro.ucsc.edu/index.html) to get a useful insight in the different aspects of how your gene might be regulated and (3) to get a sorted list of genes that share a considerable fraction of the regulatory transcription factors of your gene of interest.

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene



2. Select the desired P-value cutoff
    - 0.10 corresponds to the 10% Sg top-scoring TFs
    - 0.05 corresponds to the 5% Sg top-scoring TFs
    - 0.01 correponds to the 1% Sg top-scoring TFs

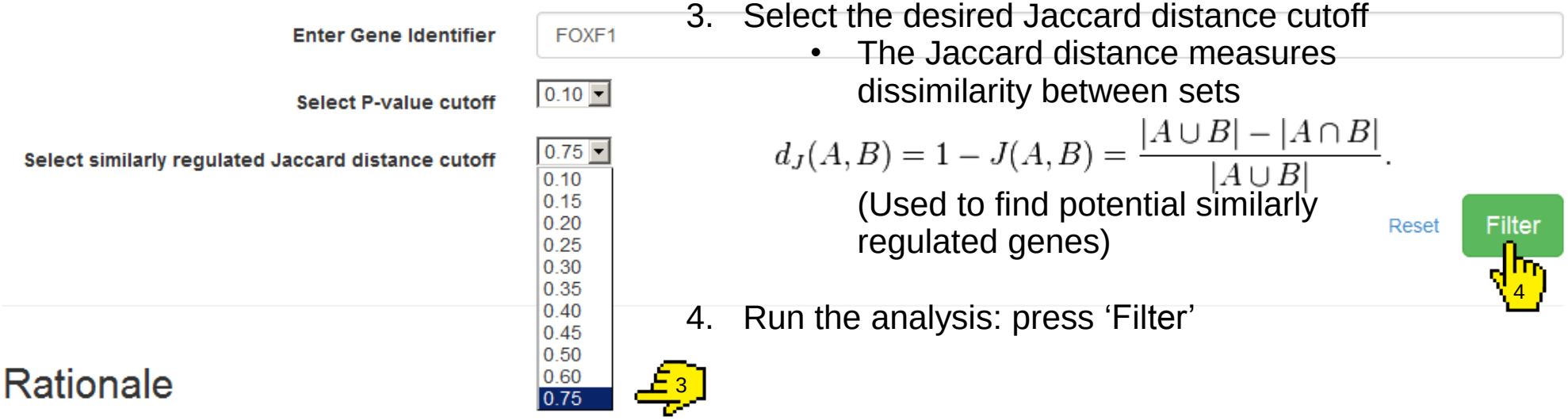
Rationale

A cistrome can be defined as a set of cis-acting elements bound by a trans-acting factor (aka transcription factor) at the genomic scale. Cistromes as such correspond to binding sites identified by ChIP-Seq experiments (Tang et al, http://cancerres.aacrjournals.org/content/71/22/6940 A major challenge is to link cistromes (or binding sites of a transcription factor) with direct target genes of that factor. However, binding sites identified by ChIP-Seq are not only found in the promoter regions of a gene but also in distal intergenic region or introns. They may contribute to regulation of gene expression through long-distance chromatin interactions. These long-distance chromatin interactions are typically studied by Hi-C, a method that probes the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing (Lieberman-Aiden et al, http://www.sciencemag.org/content/326/5950/289), and ChIA-PET, a combination of the existing methods of chromatin immunoprecipitation (ChIP) and paired-end ditag (PET) sequencing (Fullwood et al, http://www.nature.com/nature/journal/v462/n7269/full/nature08497.html). While these methods are not able to link a transcription factor binding site to its target gene, they clearly showed that interactions within single chromosomal arms exhibit in a predictable way a decrease of the contact probability P with genomic distances (Dekker et al, http://www.nature.com/nrg/journal/v14/n6/full/nrg3454.html).

Based on the findings that (1) enhancer regulation potential is proportional to the number of binding sites near a gene and (2) that the trend of chromatin interactions diminishes in a predictable way with increasing genomic distance, Tang et al (http://cancerres.aacrjournals.org/content/71/22/6940) proposed to calculate the regulatory potential of a transcription factor for a given gene as the sum of the nearby binding sites weighted by the distance from each site to the transcription start site (TSS) of the gene.

We have adapted this method and calculated for each of the 161 transcription factors contained in the ENCODE TFBS ChIP-Seq data sets, their regulatory potential on each of the 25635 genes annotated in the human hg19 genome assembly. Tyrant Cistrome allows you (1) to identify the transcription factors having the highest regulatory potential for your gene of interest, (2) to visualize the associated ChIP-Seq peak regions for these regulatory transcription factors together with the integrated regulation from ENCODE tracks of UCSC genome (http://genome-euro.ucsc.edu/index.html) to get a useful insight in the different aspects of how your gene might be regulated and (3) to get a sorted list of genes that share a considerable fraction of the regulatory transcription factors of your gene of interest.

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene



3. Select the desired Jaccard distance cutoff
   - The Jaccard distance measures dissimilarity between sets

$$d_J(A,B) = 1 - J(A,B) = \frac{|A \cup B| - |A \cap B|}{|A \cup B|}.$$

   (Used to find potential similarly regulated genes)

4. Run the analysis: press 'Filter'

Rationale

A cistrome can be defined as a set of cis-acting elements bound by a trans-acting factor (aka transcription factor) at the genomic scale. Cistromes as such correspond to binding sites identified by ChIP-Seq experiments (Tang et al, http://cancerres.aacrjournals.org/content/71/22/6940 A major challenge is to link cistromes (or binding sites of a transcription factor) with direct target genes of that factor. However, binding sites identified by ChIP-Seq are not only found in the promoter regions of a gene but also in distal intergenic region or introns. They may contribute to regulation of gene expression through long-distance chromatin interactions. These long-distance chromatin interactions are typically studied by Hi-C, a method that probes the three-dimensional architecture of whole genomes by coupling proximity-based ligation with massively parallel sequencing (Lieberman-Aiden et al, http://www.sciencemag.org/content/326/5950/289), and ChIA-PET, a combination of the existing methods of chromatin immunoprecipitation (ChIP) and paired-end ditag (PET) sequencing (Fullwood et al, http://www.nature.com/nature/journal/v462/n7269/full/nature08497.html). While these methods are not able to link a transcription factor binding site to its target gene, they clearly showed that interactions within single chromosomal arms exhibit in a predictable way a decrease of the contact probability P with genomic distances (Dekker et al, http://www.nature.com/nrg/journal/v14/n6/full/nrg3454.html).

Based on the findings that (1) enhancer regulation potential is proportional to the number of binding sites near a gene and (2) that the trend of chromatin interactions diminishes in a predictable way with increasing genomic distance, Tang et al (http://cancerres.aacrjournals.org/content/71/22/6940) proposed to calculate the regulatory potential of a transcription factor for a given gene as the sum of the nearby binding sites weighted by the distance from each site to the transcription start site (TSS) of the gene.

We have adapted this method and calculated for each of the 161 transcription factors contained in the ENCODE TFBS ChIP-Seq data sets, their regulatory potential on each of the 25635 genes annotated in the human hg19 genome assembly. Tyrant Cistrome allows you (1) to identify the transcription factors having the highest regulatory potential for your gene of interest, (2) to visualize the associated ChIP-Seq peak regions for these regulatory transcription factors together with the integrated regulation from ENCODE tracks of UCSC genome (http://genome-euro.ucsc.edu/index.html) to get a useful insight in the different aspects of how your gene might be regulated and (3) to get a sorted list of genes that share a considerable fraction of the regulatory transcription factors of your gene of interest.

The resulting output has three parts:
(1) a list of TFs with the highest regulatory potential

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier FOXF1

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

1

FOXF1 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)	
1	CTBP2	0.00556943576931085	
2	EZH2 !!!	0.00823028583012366	(FOXF1 is a known EZH2 target)
3	SUZ12	0.0087244007714207	
4	CHD1	0.037534739251267	
5	TBP	0.0535957123430126	
6	CTCF	0.0868785616034584	

(2) the associated TFBS ENCODE Peaks

FOXF1 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	CTBP2	0.00556943576931085
2	EZH2	0.00823028583012366
3	SUZ12	0.0087244007714207
4	CHD1	0.037534739251267
5	TBP	0.0535957123430126
6	CTCF	0.0868785616034584

Possible actions:

1. Show/Hide dataset
2. Download the associated peaks in bed format for downstream analysis

3. **Visualize the associated peaks in the UCSC Genome Browser**

2

FOXF1 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

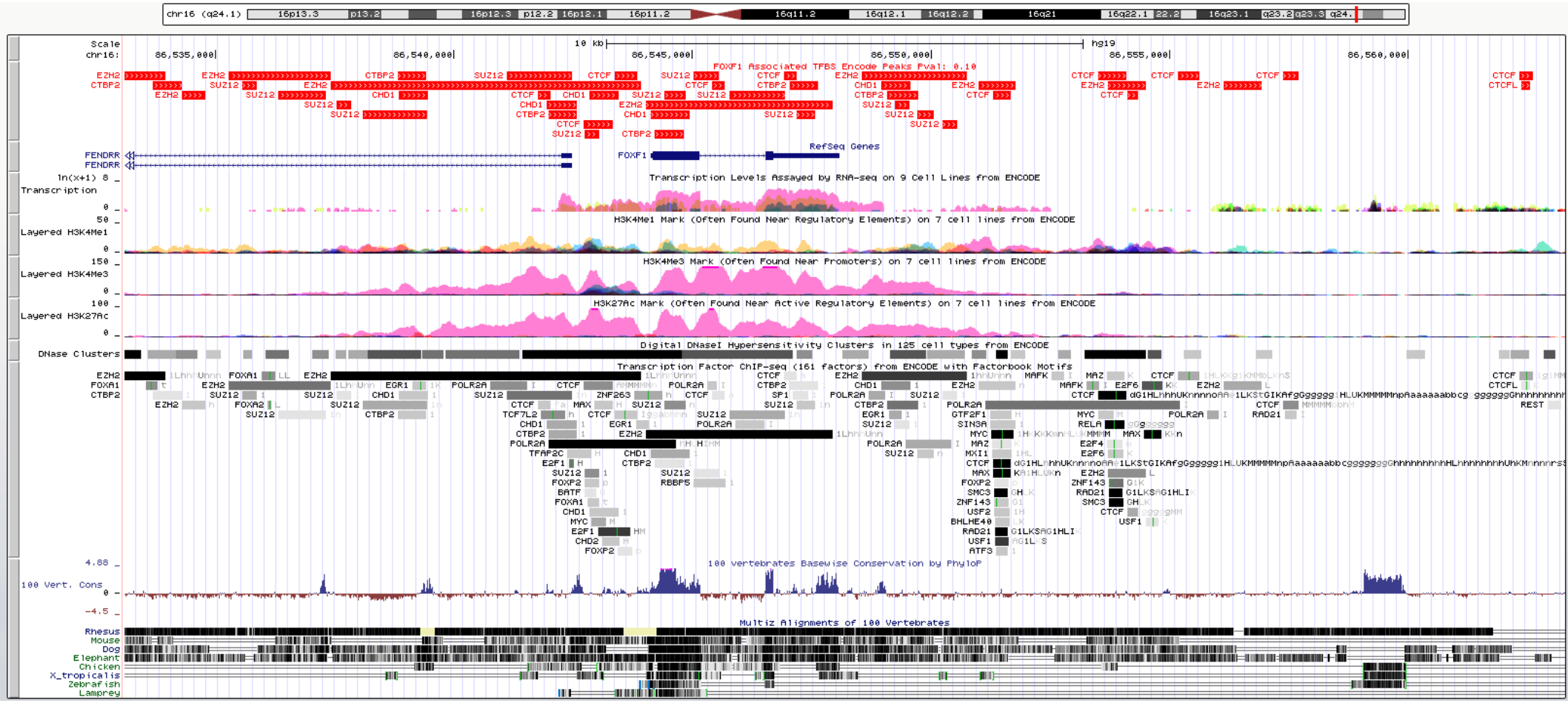
Get Flat File or Show/Hide dataset

Visualize at UCSC Genome Browser

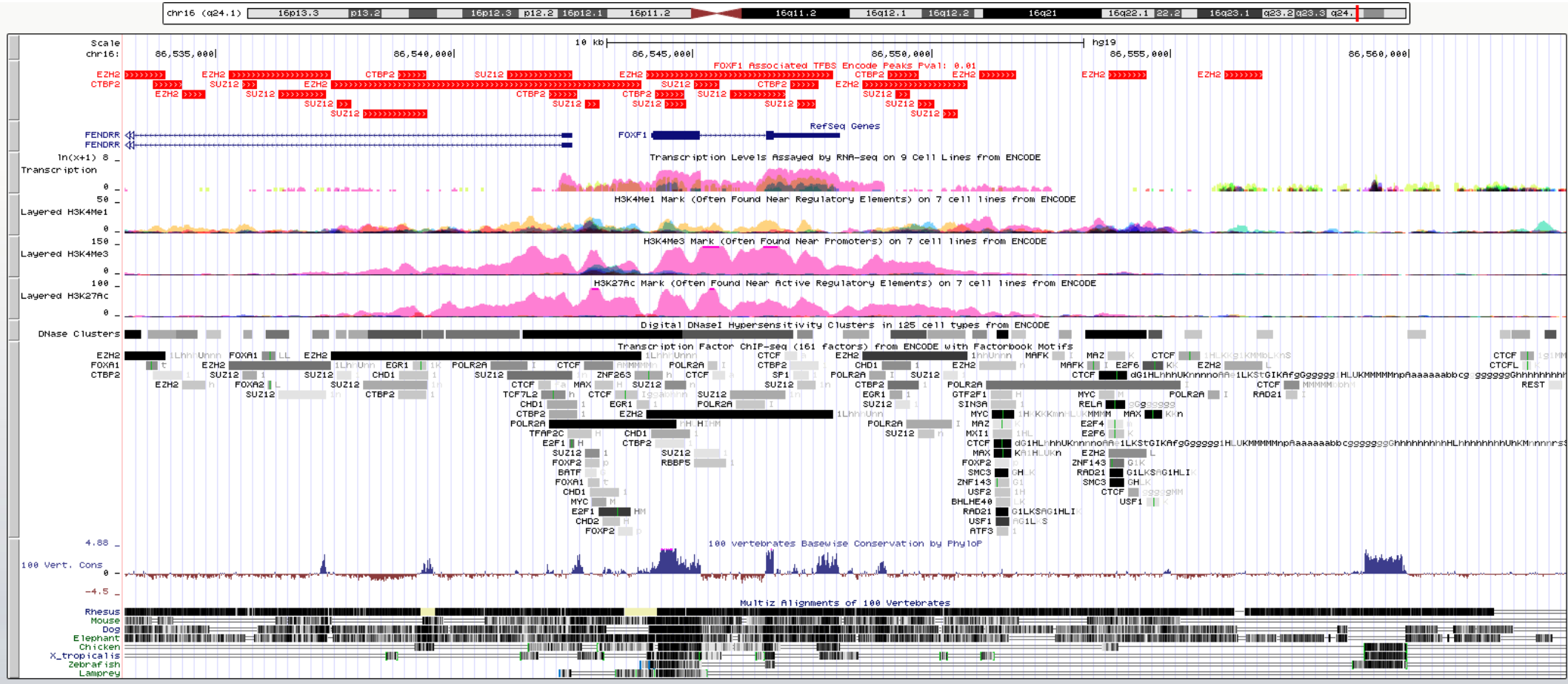
Genes putatively similarly regulated to FOXF1

Filters: Filter Table By Gene Identifiers (space seperated)

Visualization: effect of choosing different P-values (0.10)



Visualization: effect of choosing different P-values (0.01)



(3) a list of genes sharing top-scoring Sg TFs

FOXF1 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

3

Genes putatively similarly regulated to FOXF1

Filters: Filter Table By Gene Identifiers (space seperated)

1

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	FOXF1	0	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
2	OTP	0.166666666666667	CHD1, CTBP2, EZH2, SUZ12, TBP
3	UNCX	0.166666666666667	CHD1, CTBP2, EZH2, SUZ12, TBP
4	CCDC140	0.166666666666667	CHD1, CTBP2, EZH2, SUZ12, TBP
5	PAX3	0.166666666666667	CHD1, CTBP2, EZH2, SUZ12, TBP
6	ZIC4	0.25	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
7	DKFZp686K1684	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
8	PAX6	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
9	SIM2	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
10	HLX	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
11	PAX9	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
12	ZIC1	0.285714285714286	CHD1, CTBP2, EZH2, SUZ12, TBP
13	GRID1	0.333333333333333	CTBP2, CTCF, EZH2, SUZ12

2

Possible actions:

1. Filter table by Gene Identifiers
2. Run a cistrome analysis on a selected gene

Possible actions:
(1) Filter Table by Gene Identifiers

FOXF1 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to FOXF1

Filters: CTCF

1

#	Ge	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	FOXF1	0	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
6	ZIC4	0.25	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
13	GRID1	0.333333333333333	CTBP2, CTCF, EZH2, SUZ12
14	FOXD2	0.333333333333333	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
39	FOXD2-AS1	0.444444444444444	CTBP2, CTCF, EZH2, SUZ12, TBP
93	LMX1B	0.555555555555556	CTBP2, CTCF, EZH2, SUZ12
105	GATA5	0.555555555555556	CTBP2, CTCF, EZH2, SUZ12
110	WNT11	0.571428571428572	CTCF, EZH2, SUZ12
113	ATP6V1B1	0.571428571428572	CTBP2, CTCF, SUZ12

Possible actions:
(2) Run a Cistrome Analysis on a selected gene

FOXF1 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to FOXF1

Filters: CTCF

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	FOXF1	0	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
6	ZIC4	0.25	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
13	GRID1	0.333333333333333	CTBP2, CTCF, EZH2, SUZ12
14	FOXD2	0.333333333333333	CHD1, CTBP2, CTCF, EZH2, SUZ12, TBP
39	FOXD2-AS1	0.444444444444444	CTBP2, CTCF, EZH2, SUZ12, TBP
93	LMX1B	0.555555555555556	CTBP2, CTCF, EZH2, SUZ12
105	GATA5	0.555555555555556	CTBP2, CTCF, EZH2, SUZ12
110	WNT11	0.571428571428572	CTCF, EZH2, SUZ12
113	ATP6V1B1	0.571428571428572	CTBP2, CTCF, SUZ12

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier ZIC4

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Note:
The analysis uses by default the same parameters as the original analysis.

Reset Filter

ZIC4 is putatively regulated by following TFs with highest regulatory potential

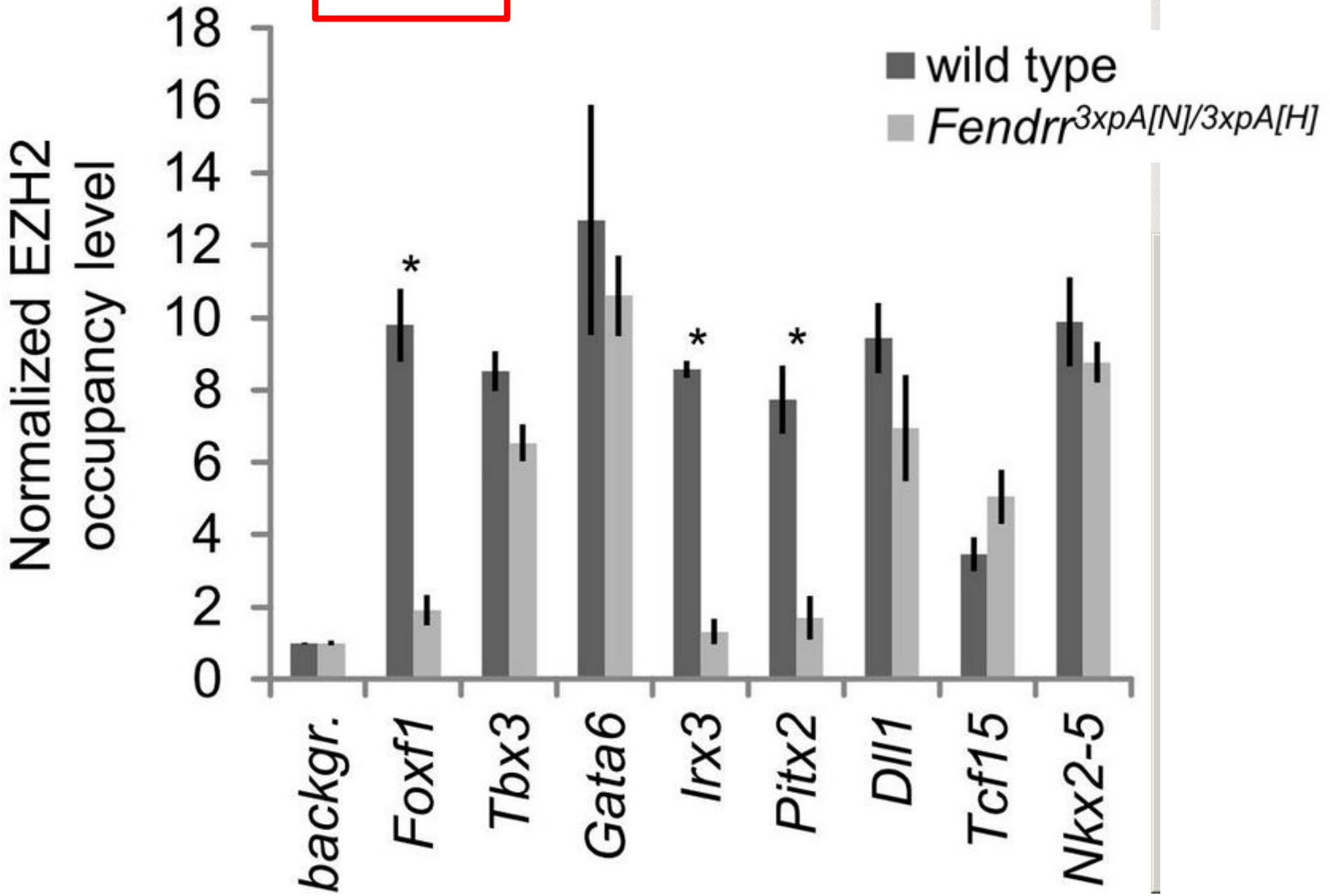
#	TF	Confidence (P-Value)
1	EZH2	0.00170281775795662
2	CTBP2	0.00218613366645846
3	SUZ12	0.0118468178896134
4	TBP	0.0159187265018799
5	POU5F1	0.0296774193548387
6	CHD1	0.0335785515775707
7	CTCF	0.0847415995283946
8	RAD21	0.0872049873831082

ZIC4 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

Positive control - Quantitative comparison of the levels of EZH2 bound to promoters.



ChIP analysis (n = 2), means ± SD, *p ≤ 0.05.

Grote P, Wittler L, Hendrix D, Koch F, Währisch S, Beisaw A, Macura K, Bläss G, Kellis M, Werber M, Herrmann BG. The tissue-specific lncRNA Fendrr is an essential regulator of heart and body wall development in the mouse. Dev Cell. 2013 Jan 28;24(2):206-14.

TBX3

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier TBX3

Select P-value cutoff 0.02

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

TBX3 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	EZH2	0.00445976079464829
2	CTBP2	0.00478867374557568
3	SUZ12	0.01129580310405

TBX3 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

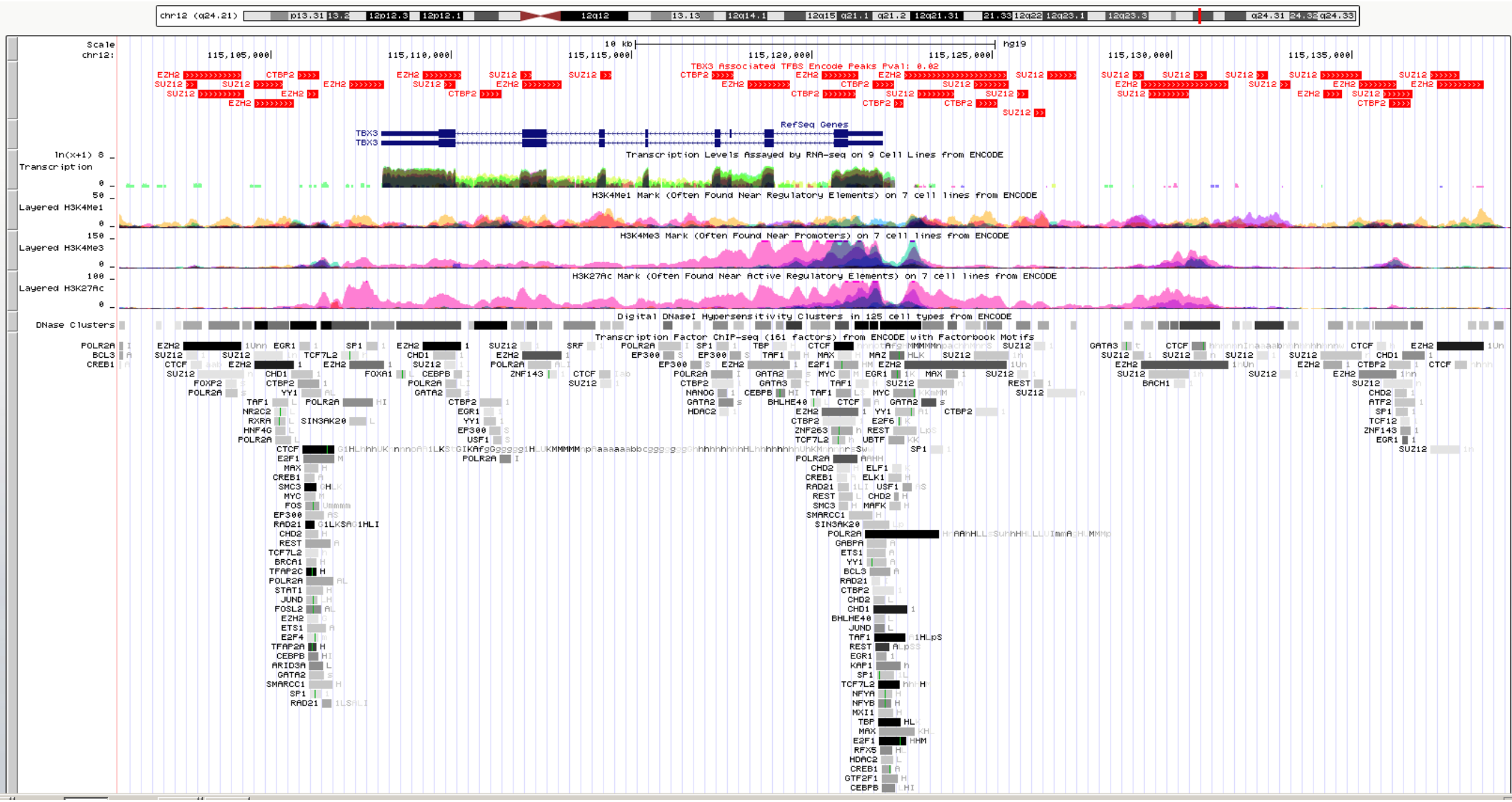
Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to TBX3

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	VAX2	0	CTBP2, EZH2, SUZ12
2	UNCX	0	CTBP2, EZH2, SUZ12
3	POU3F3	0	CTBP2, EZH2, SUZ12

TBX3 – Genomic context (hg19)



GATA6

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier GATA6

Select P-value cutoff 0.05

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

GATA6 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	EZH2	0.0226231502128522
2	SUZ12	0.0233262925888511
3	KAP1	0.0277586258580893
4	E2F1	0.0297020791455402

GATA6 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to GATA6

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	GATA6	0	E2F1, EZH2, KAP1, SUZ12
2	NKX2-3	0.25	EZH2, KAP1, SUZ12

GATA6 – Genomic context (hg19)

IRX3

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier IRX3

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

IRX3 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	CTBP2	0.0155111388715386
2	RBBP5	0.0359364201796821
3	SUZ12	0.0735604738727156
4	E2F1	0.0914464012480874
5	EZH2	0.091789985809852

IRX3 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

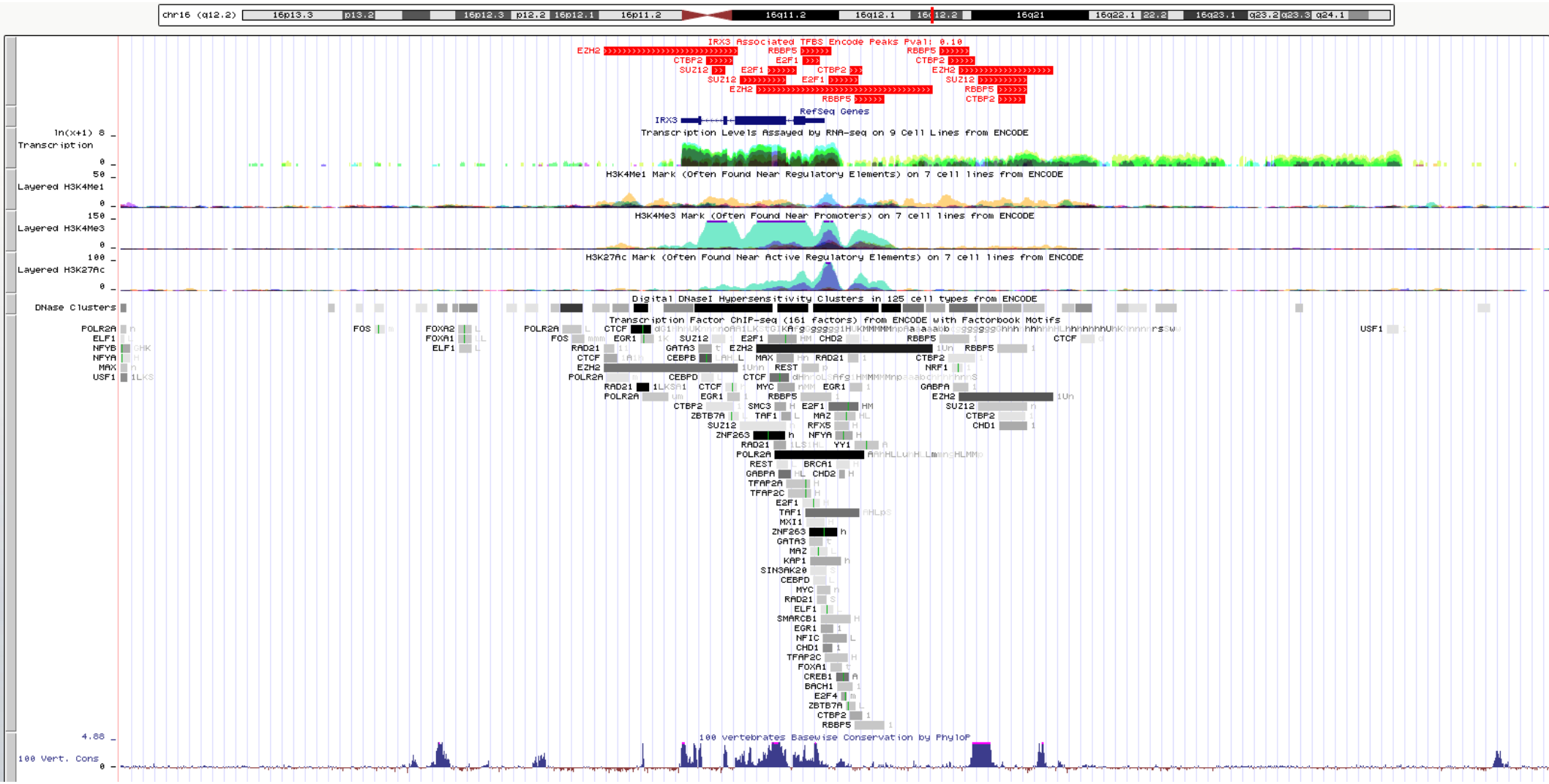
Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to IRX3

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	IRX3	0	CTBP2, E2F1, EZH2, RBBP5, SUZ12
2	HPSE2	0.2	CTBP2, EZH2, RBBP5, SUZ12
3	OLIG3	0.2	CTBP2, EZH2, RBBP5, SUZ12

IRX3 – Genomic context (hg19)



PITX2

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier PITX2

Select P-value cutoff 0.05

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

PITX2 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	CTBP2	0.002810743285446 6
2	EZH2	0.00802756943036692
3	SUZ12	0.0245201579575719
4	TBP	0.0383969282457403
5	BACH1	0.0497114957833999

PITX2 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

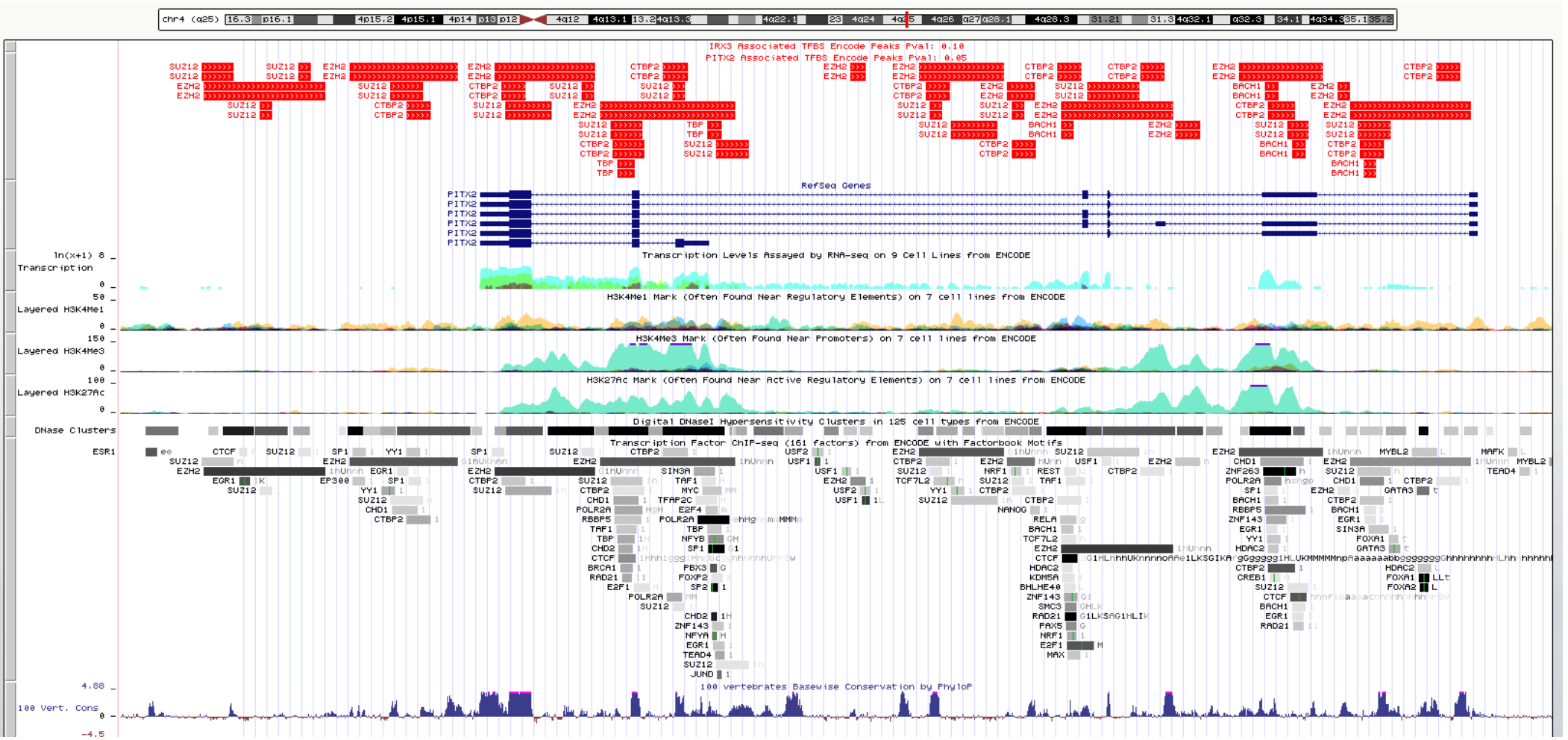
Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to PITX2

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	HOXD12	0	BACH1, CTBP2, EZH2, SUZ12, TBP
2	PITX2	0	BACH1, CTBP2, EZH2, SUZ12, TBP
3	HOXD13	0	BACH1, CTBP2, EZH2, SUZ12, TBP

PITX2 – Genomic context (hg19)



DLL1

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier DLL1

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

DLL1 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	EZH2	0.0114332049462802
2	KAP1	0.0253304955184508
3	SETDB1	0.0348250662872664
4	BACH1	0.064358632933866
5	E2F1	0.0782154750832558
6	ZNF263	0.0888287546326254

DLL1 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

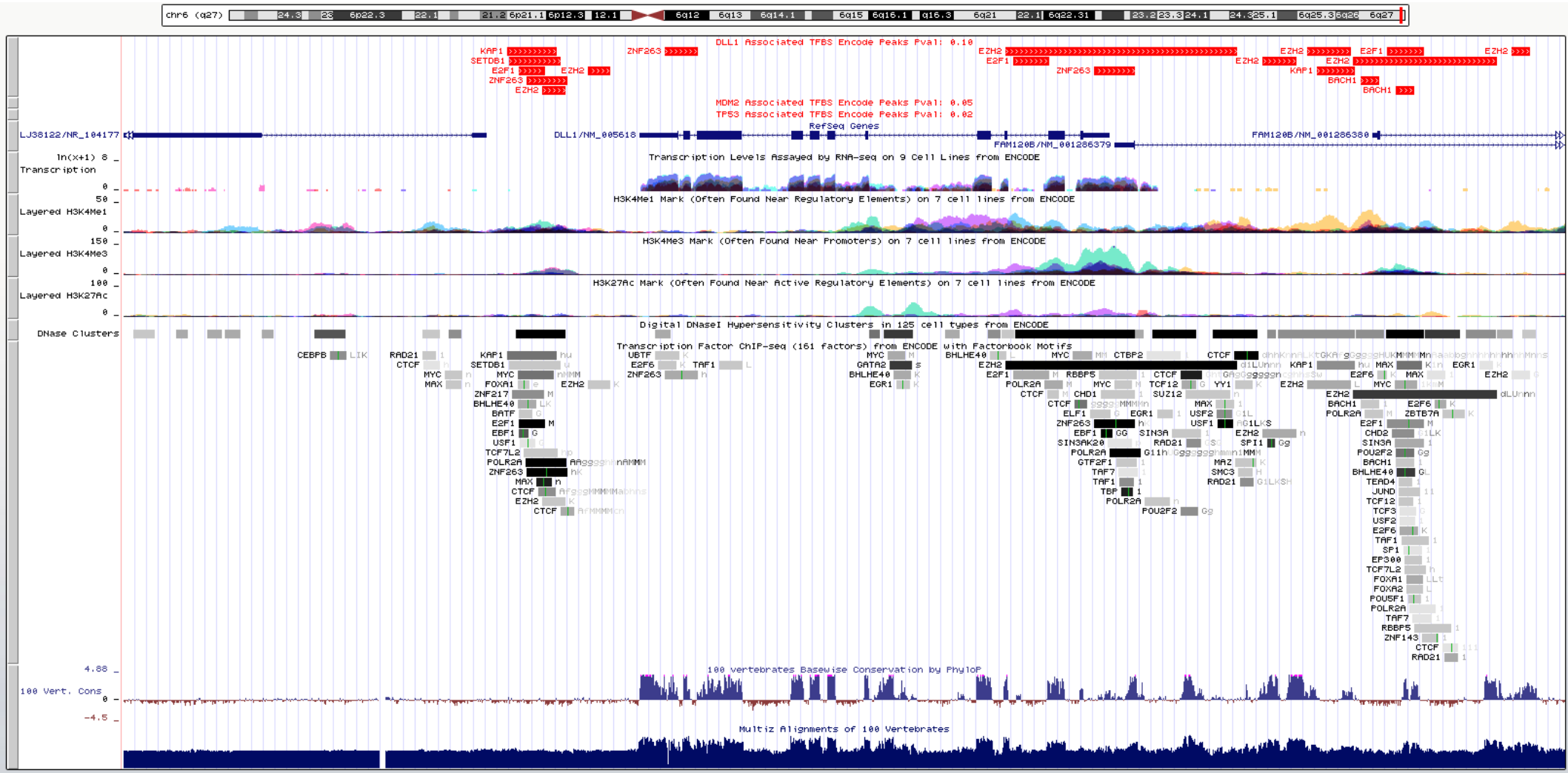
Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to DLL1

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	DLL1	0	BACH1, E2F1, EZH2, KAP1, SETDB1, ZNF263
2	KRTAP10-1	0.333333333333333	BACH1, EZH2, KAP1, SETDB1

DLL1 – Genomic context (hg19)



TCF15

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier TCF15

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

TCF15 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	EZH2	0.074194202310967

TCF15 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

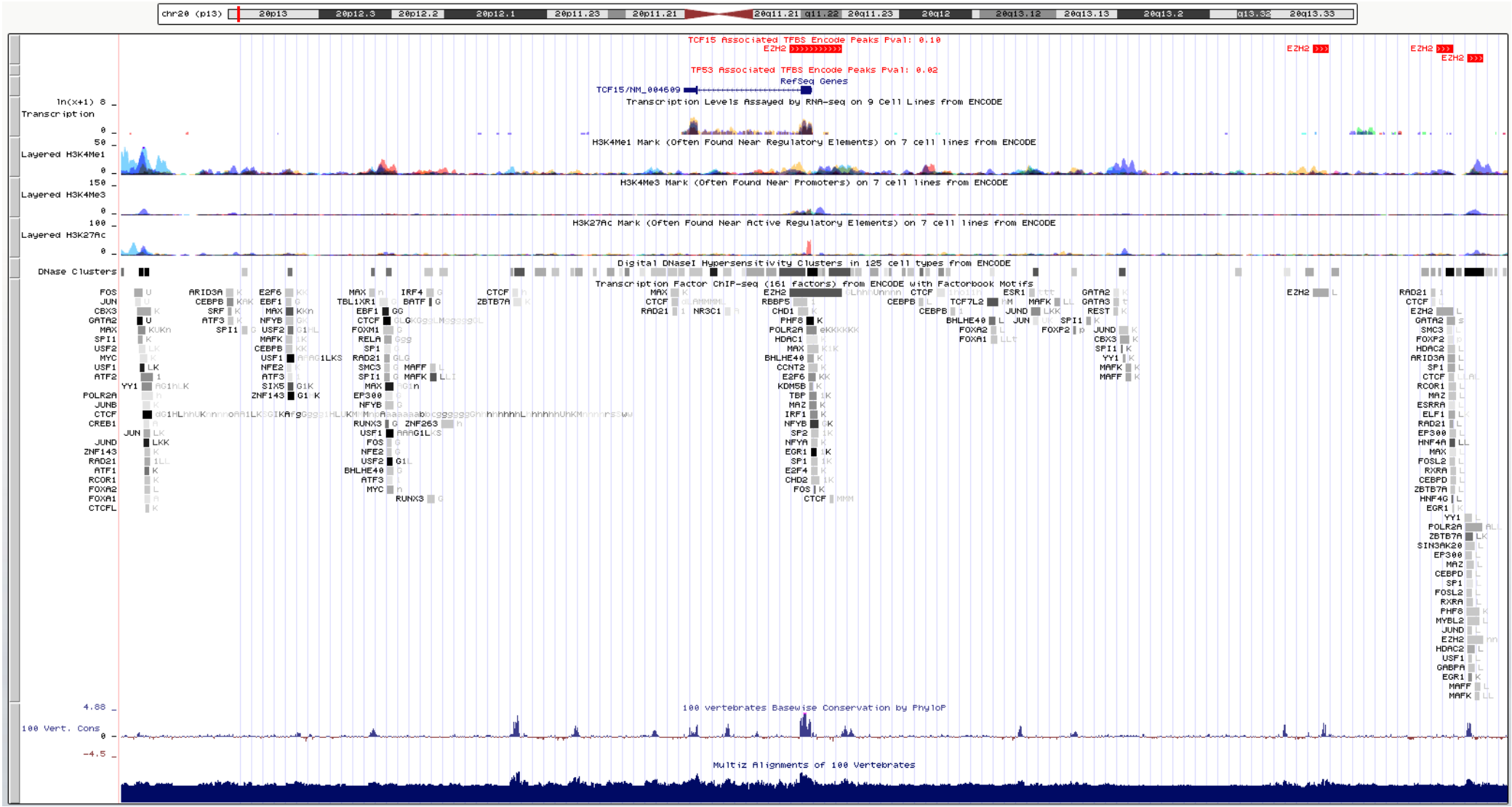
Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to TCF15

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	MIR1233-2	0	EZH2
2	FAT4	0	EZH2

TCF15 – Genomic context (hg19)



NKX2-5

Tyrant Cistrome -- Identify the Cistrome that Regulates the Expression of your Gene

Enter Gene Identifier NKX2-5

Select P-value cutoff 0.10

Select similarly regulated Jaccard distance cutoff 0.75

Reset Filter

NKX2-5 is putatively regulated by following TFs with highest regulatory potential

#	TF	Confidence (P-Value)
1	SUZ12	0.0133161906511158
2	EZH2	0.0180012162983985
3	CTBP2	0.0316468873620654

NKX2-5 Associated TFBS ENCODE Peaks With Highest Cumulative Regulatory Potential

Get Flat File or Show/Hide dataset

Visualize at UCSC-Genome Browser

Genes putatively similarly regulated to NKX2-5

Filters: Filter Table By Gene Identifiers (space seperated)

#	Gene	Jaccard Distance	Top-scoring Regulatory Potential TFs in common
1	GSX1	0	CTBP2, EZH2, SUZ12
2	TBR1	0	CTBP2, EZH2, SUZ12

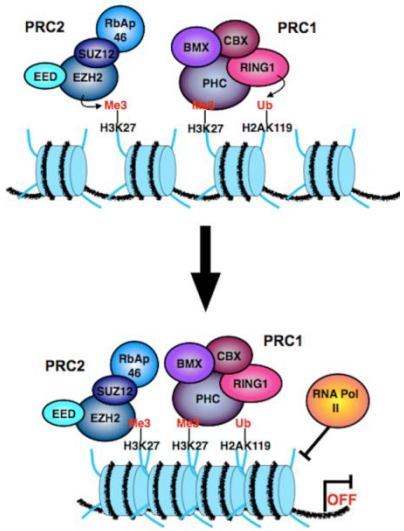
NKX2-5 – Genomic context (hg19)

Conclusions

1. Tyrant cistrome identifies in 8/8 cases EZH2 has a top ranking TF with high regular potential for the target gene.

2. Additionally, in 6/8 cases SUZ12 is identified.

3. In 5/8 cases CTBP2 is pointed to as an extra partner.



EZH2 and SUZ12 are subunits of Polycomb repressive complex 2 (PRC2), which is responsible for the repressive histone 3 lysine 27 trimethylation (H3K27me3) chromatin modification.