### *Cistrome Project* An Integrative Platform to Analyze ChIP-chip/seq Data

*Tao Liu* X. Shirley Liu lab

Department of Biostatistics and Computational Biology Dana-Farber Cancer Institute Harvard School of Public Health

## The Cistrome

- cis-acting targets of a transacting factor on a genome scale.
- Cistrome defines the genomic locations where the regulatory protein-DNA interactions occur, such as TF binding, epigenetic modification and nucleosome occupancy.





**GeneChip**<sup>®</sup>

ChIP





Next Generation Sequencing

Sunday, May 16, 2010



Sequencing

And more...

#### X. Shirley Liu Lab

DANA-FARBER

HARVARD SCHOOL OF

#### Software

- <u>Nucleosome Positioning from Sequencing (NPS)</u>
   A signal processing-based algorithm for identifying positioned nucleosomes fromsequencing experiments at the nucleosome level
- <u>Model-based Analysis of ChIP-Seq (MACS)</u> A model-based algorithm for finding enriched regions in ChIP-Seq experiments
- <u>extreme MApping of OligoNucleotides (xMAN)</u>
   A simple and efficient method for the mapping of millions of queryoligonucleotide fragments to the subject genome of any
   given length, at leastan order of magnitude faster than other popular existing tools
- <u>Model-based Analysis of 2-Color Arrays (MA2C)</u> A model-based algorithm for analyzing 2-color microarrays.
- <u>Microarray Blob Remover (MBR)</u> A microarray JAVA tool which allows rapid visualization, detection, and removalof blob-like defects as an initial quality control step
- <u>Cis-regulatory Element Annotation System(CEAS) Standalone version</u> A standalone Python package for analyzing ChIP-chip/seq data
- <u>Cis-regulatory Element Annotation System(CEAS)</u> An integrated webserver for analyzing ChIP-chip data
- <u>Model-based Analysis of Tiling-array (MAT)</u>
   A model-based algorithm for finding enriched regions in ChIP-Chip experiments
- <u>CompareProspector</u> A sequence motif-finding algorithm
- <u>Motif Regressor</u> A program for finding DNA sequence motifs
- <u>MDscan</u>
   A Fast and Accurate Motif Finding Algorithm With Applications To Chromatin Immunoprecipitation Microarray Experiments
- <u>BioProspector</u>
   Discovering Conserved DNA Motifs in Upstream Regulatory Regions of Co-ExpressedGenes

### A series of our in-house tools

## Challenges

#### • User experience

Sufficient computation power and storage

• Data availability

Sunday, May 16, 2010

## Challenges

- User experience
  - Web applications to ease the downstream data analysis for both experimental and computational biologists -- Galaxy
- Sufficient computation power and storage
  - Deploy it in the Cloud
- Data availability
  - Collect public available genome scale ChIP-chip/seq data.

### cistrome.org

#### Cistrome DC Data Collection

Cistrome AP Analysis Pipeline

Cistrome wiki Documentation Genome Browser

## cistrome.org

Cistrome DC Cistrome AP Data Cloud computing Specific Pipeline

Amazon EC2

Cist Aspera File Transfer me Documen orowser

### Cistrome DC

| 2 KW 107 Mars   | roject   |   |                             | olle    | ctio   | n <sup>V1.</sup>                                 | 1         |
|---|--|---|-----------------------------|---------|--------|--|-----------|
| Main Browse Export Manage Admir   | Experiment Files He  |   | taoliu                      | Log out | _      |  |           |
| Series Search<br>Lah: Hendrik PML-R   | ARalpha RXR Alters th  | Samples Search<br>Species:  |                             |         |        |  |           |
| Tide:   |  | Assembly:   |                             |         | _      |  |           |
| The Available Filters:  | Can Can  |   |                             |         |        |  |           |
| All Species<br>C. elegans<br>Homo Sapiens<br>Homo sapiens<br>Human<br>fake species  | All Cells<br>Cell Type_Karyoty<br>H1299_Deletion o<br>K-S62_Leukemia,<br>LB11.Sp_Lymphos<br>NB4/cancer/Leuke | f TP53<br>chronic<br>arcoma   | FBS     PMI     PMI     SIR | /N/A    | 05741  |  |           |
| The Available Series:<br>PHF8 targets histone methylation and RN<br>PML-RARalpha RXR Alters the Epigenetic<br>Pol II and its associated epigenetic marks<br>SIRT6 binding sites in KS62 cells | A FOR P<br>Laro Tide E<br>and P  | Information:<br>ML-RARalpha RXR Alte<br>pigenetic Landscape in A<br>yomyelocytic Leukemia.<br>Jendrik Stunnenberg | Acute                       | GEO     | 1005   | 6 ExtLink  |           |
| Tbx3 improves the germ-line competenc   | Pubmed 2   |   |                             | ArrayE  | 100000 | Status   | Paper     |
|   |  |   |                             |         |        |  | submitted |
| The Sample List:<br>human NB4/cancer/Leukemia PML/N/A   |  | le Information:   |                             |         | -      |  |           |
| memory concert becoming PML/N/A   | Cell P<br>Factor   | suman<br>NB4/cancer/Leukemia_H<br>PML/N/A<br>Ilumina Genome Analyz  | 150                         | Peak    | Down!  | load View<br>load View<br>load View<br>load View |           |

- Published Data collected from GEO/ ArrayExpress/author's website.
- Functions for browsing and searching.
- Collaborating project unpublished data, protected by password.





| PROFESSION STATE | -   |  |
|------------------|---|--|
| lownol .         |   |  |
| ISSN             | Char(200)   |  |
| title            | Char(300)   |  |
| factor           | Float   |  |
|                  |   |  |
| ab.              |   |  |
| PI_lastname      | Char(255)   |  |
| PI_firstname     | and a state of the second s |  |
| affiliation      | Char(255)   |  |
|                  |   |  |
| Services         |   |  |
| lab              | Leb   |  |
| title            | Char(300)   |  |
| pubmed           | Integer   |  |
| geo              | Integer   |  |
| arrayexp         | Char(300)   |  |
| update_date      | Date  |  |
| submitter        | User  |  |
| admin            | User  |  |
| ext_link         | Char(1000)  |  |
| descript         | Blob  |  |
| status           | Char(200)   |  |
|                  |   |  |
| the              |   |  |
| name             | Char(200)   |  |
| pwd              | Char(300)   |  |
| role             | Char(300)   |  |
| 21267            |   |  |

| Siorep         |                       | Prost    |
|----------------|-----------------------|----------|
| sample         | Sample                | bed      |
| submitter      | User                  | spread   |
| admin          | User                  |          |
| update_date    | Date                  | -        |
| treatment_file | t Raw                 | Sub land |
| input_file     | Raw                   | wiggle   |
| peak.          | Peak                  |          |
| wiggle         | Signal                | -        |
| status         | Char(200)             | series   |
|                |                       | factor   |
| Teatree        |                       | antibo   |
| biorep         | Biorep                | specie   |
| experimenter   | Char(255)             | assem    |
| admin          | User                  | ceil     |
| submitter      | User                  | descri   |
| update_date    | Date                  | expres   |
| treatment_file | c Raw                 | platfo   |
| input_file     | Raw                   | submi    |
| peak           | Peak                  | admin    |
| wiggle         | Signal                | updat    |
| status         | Char(200)             | ceas     |
| -              | 1000                  | qc       |
| 141            | Charles Charles       | peak     |
| celitype       | Char(255)             | wiggle   |
| karyotype      | Char(255)             | status   |
| source_tissue  | and the factor of the |          |
| species        | Char(200)             | Featre   |
| metastatic_sit |                       | name     |
| descript       | Blob                  | access   |

| bed         | Filepath   | typ   |
|-------------|------------|-------|
| spreadsheet | Filepath   | id    |
| Signal      |            | 100   |
| wiggle      | Filepath   | nar   |
|             |            | ma    |
| -           |            | cod   |
| Semet       | Garage R.  |       |
| series      | Series     | 1.00  |
| factor      | Factor     | nar   |
| antibody    | Antibody   | top   |
| species     | Char(200)  | mix   |
| assembly    | Char(200)  | bot   |
| cell        | Cell       | 100   |
| descript    | Biob       |       |
| expression  | Expression | 100   |
| platform    | Platform   | imi   |
| submitter   | User       |       |
| admin       | User       |       |
| update_date | Date       | 100   |
| ceas        | Ceas       | 100   |
| qc          | Qc         | spe   |
| peak        | Peak       |       |
| wiggle      | Signal     | 110.0 |
| status      | Char(200)  | nar   |
| Foctor      |            | COR   |
| name        | Char(255)  |       |
| accession   | Char(255)  |       |
| comment     | Blob       |       |
|             |            |       |

| type        | Char(200) |
|-------------|-----------|
| id          | integer   |
| Antibody    |           |
| name        | Char(255) |
| made_by     | Char(255) |
| cooment     | Blob      |
| Deressian   |           |
| name        | Char(100) |
| top10       | Text      |
| mid10       | Text      |
| bottom10    | Text      |
| raw         | Raw       |
| Øc-         |           |
| image       | Filepath  |
| Cent        | 15        |
| image       | Filepath  |
| spreadsheet | Filepath  |
| Plutform    | 1         |
| name        | Char(255) |
| company     | Char(255) |
| comment     | Blob      |

| F | ilepath   |  |
|---|-----------|--|
| F | lepath    |  |
|   | 24270.012 |  |
|   |           |  |

e 1951

bpmap cel

| Chipvantable | 900       |
|--------------|-----------|
| ndf          | Filepath  |
| pos          | Filepath  |
| 635pair      | Filepath  |
| 532pair      | Filepath  |
| Chiesellen   |           |
| data         | Filepath  |
| Feamor       |           |
| bed          | Filepath  |
| other        | Filepath  |
| Launimble    | 208       |
| data         | Filepath  |
| Expetty .    |           |
| data         | Filepath  |
| filmoth      |           |
| filepath     | File      |
| type         | Char(200) |
|              |           |



#### Peak calling -- MAT, MA2C and MACS

- Annotation and Visualization -- CEAS (sitepro, ceas, and gca) + Conservation plot + Heatmap
- Motif analysis motif discovery and motif scan
- Correlation -- e.g. many wiggle files of score profile
- Expression and GO
- Liftover and wiggle file standardization
- Import from DC and upload raw data
- Export published dataset to public DC
- Other Galaxy Low-Level Operations

# 26.4 % - 35.6 %

**Distribution of ChIP Regions** 

#### Peak calling -- MAT, MA2C and MACS

- Annotation and Visualization -- CEAS (sitepro, ceas, and gca) + Conservation plot + Heatmap
- Motif analysis motif discovery and motif scan
- Correlation -- e.g. many wiggle files of score profile
- Expression and GO
- Liftover and wiggle file standardization
- Import from DC and upload raw data
- Export published dataset to public DC
- Other Galaxy Low-Level Operations



- Peak calling -- MAT, MA2C and MACS
- Annotation and Visualization -- CEAS (sitepro, ceas, and gca) + Conservation plot + Heatmap
- Motif analysis motif discovery and motif scan
- Correlation -- e.g. many wiggle files of score profile
- Expression and GO
- Liftover and wiggle file standardization
- Import from DC and upload raw data
- Export published dataset to public DC
- Other Galaxy Low-Level Operations

| 1 Cistrome   | Analyze Data   | Workflow                           | Libraries   | Admin Help   | User                      |  |                  |
|--|--|------------------------------------|---|--|---------------------------|--|------------------|
| Tools  |  |                                    |   |  |                           | History  | Options          |
| Import Data<br>Peak Calling<br>Peak Calling - MAT<br>Correlation<br>Annotate and Visualize | The Website is under construction!<br>Thanks to your support and test for our Cistrome AP site, which is<br>based on <u>Galaxy</u> , a Metaserver for integrative analysis of genomic<br>data. Please check our project trac site <u>here</u> for more information.<br><u>64: Conservation /</u><br>Aggregate Datapoints |                                    |   |  |                           |  |                  |
| Motif<br>Liftover  | strome Ana   |                                    |   |  |                           | on data 1<br>63: Conservation /<br>Aggregate Datapoints              | • / %            |
| Galaxy:Send Data da  | e Cistrome AP mode<br>d provide users a dr<br>a. After processing<br>a and publish them  | ry-lab workbend<br>their data, use | th for them the | to process their or<br>se and package th                     | wn private<br>eir private | on data 1<br>55: Heatmap on data<br>49 and data 9                    | • / ×            |
| Galaxy:Text Manipulation pr<br>Galaxy:Filter and Sort m                                    | vate data and analy<br>cess their own data<br>dule, this is the en<br>dule.  | a, and publish t                   | hem into ou   | r Cistrome Data (  | Collection                | 54: Heatmap on data<br>49 and data 9                                 | • / X            |
| Galaxy:Convert Formats<br>Galaxy:Extract Features<br>Galaxy:Fetch Sequences                | lick Links to Tu   |                                    | blah  |  |                           | 50: Two scores for<br>whole datasets on<br>data 49, data 4, and da   | • / X            |
| Galaxy:Get Genomic Scores<br>Galaxy:Operate on Genomic<br>Intervals                        | h1   | blah2                              |   | blah3  |                           | 49:<br>Wig:AB9050_H3K36M   | ● / ☆<br>E3 N2 I |
| Far  | The Cistrome Development team is a part of Xiaole Shirley Liu's Lab at Dana-   |                                    |   |  |                           | 48: Two scores for<br>Two Intervals on data<br>2, data 5, and others | • / ×            |
|  | Farber Institute.<br>Galaxy build: <b>\$Rev 1733:a4214de3752e\$</b>  |                                    |   | 47: Two scores for<br>whole datasets on<br>data 4 and data 5 |                           |  |                  |
|  |  |                                    |   |  |                           | 44: Two scores for<br>Two Intervals on data<br>2, data 5, and others | • / %            |

#### Peak calling -- MAT, MA2C and MACS

- Annotation and Visualization -- CEAS (sitepro, ceas, and gca) + Conservation plot + Heatmap
- Motif analysis motif discovery and motif scan
- Correlation -- e.g. many wiggle files of score profile
- Expression and GO
- Liftover and wiggle file standardization
- Import from DC and upload raw data
- Export published dataset to public DC
- Other Galaxy Low-Level Operations

## Cistrome AP

| <b>2</b> Cistrome  | Analyze Data Workflow Data Libraries Admin Help User  |  |           |
|--|---|--|-----------|
| Tools  | <b>1</b> The Website is under construction!   | History  | Options 👻 |
| Import Data<br>Peak Calling<br>Peak Calling - MAT  | Thanks to your support and test for our Cistrome AP site, which is based on <u>Galaxy</u> , a Metaserver for integrative analysis of genomic data. Please check our project trac site <u>here</u> for more information.   | Unnamed history                                  | Ø 🖻       |
| Correlation<br>Annotate and Visualize<br>Expression  | Cistrome Analysis Pipeline (AP) Module  | Your history is empty<br>Data' on the left panel |           |
| Motif<br>Liftover/Others<br>Galaxy:Get Data<br>Galaxy:Send Data<br>Galaxy:Lift-Over<br>Galaxy:Text Manipulation<br>Galaxy:Filter and Sort<br>Galaxy:Join, Subtract and Group<br>Galaxy:Convert Formats | The Cistrome AP module is to organize the analysis tools in a pipeline for<br>users, and provide users a dry-lab workbench for them to process their own<br>private data. After processing their data, users can choose and package their<br>private data and publish them into Cistrome Data Collection, or they can<br>share their private data and analysis results with their friends. So if the goal<br>for users is to process their own data, and publish them into our Cistrome<br>Data Collection module, this is the entry. We choose <u>Galaxy</u> as the backbone<br>for pipeline module. |  |           |
| Galaxy:Extract Features<br>Galaxy:Fetch Sequences<br>Galaxy:Get Genomic Scores<br>Galaxy:Operate on Genomic<br>Intervals   | Tutorial on Analysis Pipeline module  |  |           |
| <u>Workflows</u>   | The Cistrome Development team specially thank Eli Lilly, Tongji University,<br>the Dana-Farber Cancer Institute and the National Institutes of Health for<br>their support.<br>Galaxy build: \$Rev 3528:48e83411aa91\$  |  |           |

## Cistrome AP

| 👥 Cistrome  | Analyze Data Workflow Data Libraries Admin Help User  |
|---|---|
| Tools   | 1 The Website is under construction! History Options -  |
| Import Data<br>Peak Calling<br>Peak Calling - MAT   | Thanks to your support and test for our Cistrome AP site, which is based on <u>Galaxy</u> , a Metaserver for integrative analysis of genomic data. Please check our project trac site <u>here</u> for more information.   |
| Correlation<br>Annotate and Visualize<br>Expression   | Cistrome Analysis Pipeline (AP) Module  |
|   | The Cistrome AP module is to organize the analysis tools in a pipeline for<br>users, and provide users a dry-lab workbench for them to process their own<br>private data. After processing their data, users can choose and package their<br>private data and publish them into Cistrome Data Collection, or they can |
| Galaxy:Lift-Over<br>Galaxy:Text Manipulation  | share their private data and analysis results with their friends. So if the goal<br>for users is to process their own data, and publish them into our Cistrome<br>Data Collection module, this is the entry. We choose <u>Galaxy</u> as the backbone<br>for pipeline module.  |
| Galaxy:Join, Subtract and Group<br>Galaxy:Convert Formats<br>Galaxy:Extract Features          | Quick Links to Tutorials  |
| Galaxy:Fetch Sequences<br>Galaxy:Get Genomic Scores<br>Galaxy:Operate on Genomic<br>Intervals | Tutorial on Analysis Pipeline module  |
| Workflows   | <u>The Cistrome Development team</u> specially thank <u>Eli Lilly, Tongji University,</u><br><u>the Dana-Farber Cancer Institute</u> and <u>the National Institutes of Health</u> for<br>their support.<br>Galaxy build: <b>\$Rev 3528:48e83411aa91\$</b>   |

#### *Cistrome* documentation & & local genome browser



SUBVERSION

Data harvest





Sunday, May 16, 2010



Sunday, May 16, 2010

## Import data to AP

#### Tools

#### Import Data

- DC data browser Public Data
- wormENCODE data browser wormENCODE ( passwd required )
- Upload File from your computer
- <u>Upload Affymetrix .CEL or</u> <u>NimbleGen .XYS files</u> from your computer

#### >600 Public ChIP-seq datasets to be added ~500 modENCODE ChIP-chip/seq

| he Available Filters:   |  |  |           |        |                                      |                      |
|---|--|--|-----------|--------|--------------------------------------|----------------------|
| VI Species(1)<br>Iomo Sapiens   | All Cells(1)<br>H1299_Deletion of TP53 All Factors(1)<br>PML |  |           |        |                                      |                      |
| he Available Series:<br>NA specificity determinants associate with distinct t<br>rythroid GATA1 function revealed by genome-wide<br>set partners with Oct4 to restrict extraembryonic tro<br>lene expression and UH2A ChIP-Seq binding analysis<br>lenome-wide profiling of PPARgamma:RXR and RNA | <b>The Ser</b><br>Title<br>Lab                               | les Information:<br>BRD7 is a candidate tumour<br>suppressor gene required for p53<br>function.<br>Peggy Farnham | GEO       | 200    | 76 ExtLink                           |                      |
|   | Pubmed   | 20228809   | ArrayI    | Exp    | AFAILIE                              | Paper<br>submitted   |
| he Sample List:   | The San  | nple Information:  |           |        |                                      |                      |
| lomo Sapiens_H1299_PML_BRD7   | Species<br>Cell<br>Factor                                    | Homo Sapiens<br>H1299_Deletion of TP53_Lung<br>PML   | Carcinoma |        | Download<br>Download<br>export to AF | View<br>View<br>View |
|   | Platform   | Illumina Genome Analyzer/Illur   | nina      | Wiggle | export to Al                         | View                 |

## Import data to AP

#### Tools

#### Import Data

- DC data browser Public Data
- wormENCODE data browser wormENCODE ( passwd required )
- Upload File from your computer
- <u>Upload Affymetrix .CEL or</u> <u>NimbleGen .XYS files</u> from your computer

#### >600 Public ChIP-seq datasets to be added ~500 modENCODE ChIP-chip/seq

| All Species(1)   | All Cells(1) All Factors(  |  |                |        |             |                    |
|--|----------------------------|--|----------------|--------|-------------|--------------------|
| Homo Sapiens   | H1299_Deletion of TP53 PML |  |                |        |             |                    |
| The Available Series:  | The Seri                   | ies Information:   |                |        |             |                    |
| DNA specificity determinants associate with distinct t<br>Erythroid GATA1 function revealed by genome-wide<br>Eset partners with Oct4 to restrict extraembryonic tro<br>Gene expression and UH2A ChIP-Seq binding analysis | Title                      | BRD7 is a candidate tumou<br>suppressor gene required for<br>function. |                |        |             |                    |
| Genome-wide profiling of PPARgamma:RXR and RNA   | Lab                        | Peggy Farnham  | GEO            | 200    | 76 ExtLink  |                    |
|  | Pubmed                     | 20228809   | ArrayI         | Sxp    | SERUIS      | Paper<br>submitted |
| The Sample List:   | The San                    | nple Information:  |                |        |             |                    |
| Homo Sapiens_H1299_PML_BRD7  | Species                    | Homo Sapiens   |                | CEAS   | Download    | View               |
|  | Cell                       | H1299_Deletion of TP53_  | Lung Carcinoma | QC     | Download    | View               |
|  | Factor                     | PML  |                | Peak   | export to A | P) View            |
|  | Platform                   | Illumina Genome Analyzer   | /Illumina      | Wiggle | export to A | P View             |

## Import data to AP

#### Tools

#### Import Data

- DC data browser Public Data
- wormENCODE data browser wormENCODE ( passwd required )
- Upload File from your computer
- <u>Upload Affymetrix .CEL or</u> <u>NimbleGen .XYS files</u> from your computer

#### >600 Public ChIP-seq datasets to be added ~500 modENCODE ChIP-chip/seq

| he Available Filters:   |  |   |                       |               |                    |  |
|---|--|---|-----------------------|---------------|--------------------|--|
| II Species(1)<br>Iomo Sapiens   | All Cells(1)<br>H1299_Deletion of TP53 | All Fa<br>PML   | All Factors(1)<br>PML |               |                    |  |
| he Available Series:<br>NA specificity determinants associate with distinct t<br>rythroid GATA1 function revealed by genome-wide<br>set partners with Oct4 to restrict extraembryonic tro<br>ene expression and UH2A ChIP-Seq binding analysis<br>enome-wide profiling of PPARgamma:RXR and RNA |  | a candidate tumour<br>or gene required for p53                | GEO 2                 | 20076 ExtLink |                    |  |
|   | Pubmed 20228809                        | 2   | ArrayExp              | ADDITIE       | Paper<br>submitted |  |
| he Sample List:   | The Sample Infor                       | mation:   |                       |               |                    |  |
| omo Sapiens_H1299_PML_BRD7  | Factor PML                             | apiens<br>Deletion of TP53_Lung Ca<br>Genome Analyzer/Illumin | Peak                  | Download      | <u>View</u>        |  |

#### Sunday, May 16, 2010



### MACS Model based Analysis of ChIP-Seq

- Tags need to be shifted and extended with a estimated fragment size.
- Model the local bias caused by open chromatin effects, or sequence mappability.



Nat Rev Genet (2009) vol. 10 (10) pp. 669-80

### MACS Model based Analysis of ChIP-Seq

- Tags need to be shifted and extended with a estimated fragment size.
- Model the local bias caused by open chromatin effects, or sequence mappability.





#### Tools

Import Data

Peak Calling

Peak Calling - MAT

Correlation

Annotate and Visualize

 <u>Sitepro: Score profile near</u> <u>Intervals</u> Draw the score profile near a given interval

 GCA: Gene centered annotation Find the nearest interval in the given intervals set fo every annotated coding gene

 <u>CEAS: Enrichment on</u> <u>chromosome and annotation</u> Annotate the given intervals and scores with genome features such as gene body

 <u>Conservation / Aggregate</u> <u>Datapoints</u> Calculates the PhastCons scores in several intervals sets

 <u>Heatmap</u> Draw the scores heatmap near a given interval set and use k-means to cluster the intervals

### CEAS

Cis-regulatory Element Annotation System

A easy solution to generate graphic report and statistics

- Published in *Bioinformatics* (2009) vol.
  25 (19) pp. 2605-6
- Coded in Python

- Chromosomal distribution of ChIP enriched regions
- Feature distribution
- Signal profiles



Chromosomal Distribution of ChIP Regions

 Chromosomal distribution of ChIP enriched regions

 Feature distribution

• Signal profiles



 Chromosomal distribution of ChIP enriched regions

 Feature distribution

• Signal profiles



 Chromosomal distribution of ChIP enriched regions

 Feature distribution

• Signal profiles



#### Signal annotation

 Chromosomal distribution of ChIP enriched regions

 Feature distribution

Signal profiles



#### Signal annotation

 Chromosomal distribution of ChIP enriched regions

 Feature distribution

Signal profiles



#### Signal annotation

 Chromosomal distribution of ChIP enriched regions

 Feature distribution

Signal profiles



## Heatmap and clustering





### Correlation

|       |   | 1           | 0.17       | -0.03            | 0.03             | -0.01            | 0.03            | 0.07   | 0.07            | -0.01             | 0.03              | 0.05              | 0.06              | 0.14             | 0.12             | 0.13             | GeneDensity         |
|-------|---|-------------|------------|------------------|------------------|------------------|-----------------|--------|-----------------|-------------------|-------------------|-------------------|-------------------|------------------|------------------|------------------|---------------------|
|       | _ | 0.17        | 1          | 0.04             | 0.26             | 0.32             | 0.56            | 0      | 0.38            | 0.23              | 0.39              | 0.15              | 0.19              | 0.29             | 0.33             | 0.32             | H3(AR0144)          |
| <br>_ | _ | -0.03       | 0.04       | 1                | 0.49             | 0.65             | 0.49            | -0.15  | -0.31           | -0.11             | -0.07             | -0.15             | -0.13             | -0.04            | -0.19            | -0.23            | H3K9me3(HK00009)    |
|       |   | 0.03        | 0.26       | 0.49             | 1                | 0.6              | 0.6             | -0.02  | -0.31           | -0.08             | -0.08             | -0.24             | -0.24             | 0.02             | -0.17            | -0.12            | H4K20me1(AB9051)    |
|       |   | -0.01       | 0.32       | 0.65             | 0.6              | 1                | 0.85            | -0.18  | -0.16           | 0                 | 0.02              | 0.01              | 0.08              | -0.08            | -0.07            | -0.14            | H3K9me2(HK00008)    |
|       |   | 0.03        | 0.56       | 0.49             | 0.6              | 0.85             | 1               | -0.18  | 0.03            | 0.11              | 0.22              | -0.01             | 0.07              | 0.05             | 0.06             | 0.02             | H3K9me1(AB9045)     |
|       |   | 0.07        | 0          | -0.15            | -0.02            | -0.18            | -0.18           | 1      | 0.22            | 0.19              | 0.14              | 0.38              | 0.31              | 0.42             | 0.38             | 0.41             | RNAseq              |
|       |   | 0.07        | 0.38       | -0.31            | -0.31            | -0.16            | 0.03            | 0.22   | 1               | 0.73              | 0.82              | 0.56              | 0.57              | 0.68             | 0.72             | 0.76             | H3K27ac(AB4729)     |
|       |   | -0.01       | 0.23       | -0.11            | -0.08            | 0                | 0.11            | 0.19   | 0.73            | 1                 | 0.76              | 0.43              | 0.42              | 0.59             | 0.52             | 0.62             | H3K4me3(WA30534819) |
|       | L | 0.03        | 0.39       | -0.07            | -0.08            | 0.02             | 0.22            | 0.14   | 0.82            | 0.76              | 1                 | 0.33              | 0.34              | 0.64             | 0.56             | 0.66             | H3K4me2(WA30834809) |
|       |   | 0.05        | 0.15       | -0.15            | -0.24            | 0.01             | -0.01           | 0.38   | 0.56            | 0.43              | 0.33              | 1                 | 0.97              | 0.63             | 0.8              | 0.73             | H3K36me3(HK00001)   |
|       |   | 0.06        | 0.19       | -0.13            | -0.24            | 0.08             | 0.07            | 0.31   | 0.57            | 0.42              | 0.34              | 0.97              | 1                 | 0.6              | 0.79             | 0.72             | H3K36me2(HK00012)   |
|       |   | 0.14        | 0.29       | -0.04            | 0.02             | -0.08            | 0.05            | 0.42   | 0.68            | 0.59              | 0.64              | 0.63              | 0.6               | 1                | 0.8              | 0.95             | H3K79me3(AB2621)    |
|       |   | 0.12        | 0.33       | -0.19            | -0.17            | -0.07            | 0.06            | 0.38   | 0.72            | 0.52              | 0.56              | 0.8               | 0.79              | 0.8              | 1                | 0.89             | H3K79me1(AB2886)    |
|       | L | 0.13        | 0.32       | -0.23            | -0.12            | -0.14            | 0.02            | 0.41   | 0.76            | 0.62              | 0.66              | 0.73              | 0.72              | 0.95             | 0.89             | 1                | H3K79me2(AB3594)    |
|       |   | GeneDensity | H3(AR0144) | H3K9me3(HK00009) | H4K20me1(AB9051) | H3K9me2(HK00008) | H3K9me1(AB9045) | RNAseq | H3K27ac(AB4729) | K4me3(WA30534819) | K4me2(WA30834809) | H3K36me3(HK00001) | H3K36me2(HK00012) | H3K79me3(AB2621) | H3K79me1(AB2886) | H3K79me2(AB3594) |                     |







### Motif Analysis SeqPos



id:M00481 factor:AR consensus:1G1AC5G2C1 hits:6774 cutoff:3.2452 zscore:-53.0853 -10\*log(pval):1e-30 position:-0.1362 show motif in new window

| click to reset table |           |             |       |             |          |                    |
|----------------------|-----------|-------------|-------|-------------|----------|--------------------|
| id~                  | factor    | consensus   | hits~ | cutoff<br>~ | zscore×  | -10*log(pval)<br>~ |
| M00481               | AR        | 1G1AC5G2C1  | 6774  | 3.2452      | -53.0853 | 1e-30              |
| M00481_observed      | AR        | 1G1AC5G2C1  | 6774  | 3.2452      | -53.0853 | 1e-30              |
| M00921_observed      | GR        | WCTGTYCT    | 26679 | 3.81        | -52.0571 | 1e-30              |
| M00921               | GR        | WSTGTYCT    | 26679 | 3.81        | -52.0571 | 1e-30              |
| M00724               | HNF3alpha | HWRARYAAAYA | 10842 | 4.785       | -49.2657 | 1e-30              |
| M00724_observed      | HNF3alpha | HWRWRYAAAYA | 10842 | 4.785       | -49.2657 | 1e-30              |
| M00956               | AR        | 6AGAAC16    | 5159  | 3.0003      | -46.6236 | 1e-30              |
| M00956_observed      | AR        | 6AG1ACA15   | 5159  | 3.0003      | -46.6236 | 1e-30              |
| M00955_observed      | GR        | 6AG1ACA15   | 9458  | 3.0015      | -45.8589 | 1e-30              |
| M00955               | GR        | 6AGAAC16    | 9458  | 3.0015      | -45.8589 | 1e-30              |

#### Seqpos motif tool

| BED file (at most 10K lines):          |  |
|--|--|
| Genome Assembly in UCSC:               |  |
| hg18 \$                                |  |
| Select which motif database(s) to use: |  |
| Select All Unselect All                |  |
| 🗌 pbm                                  |  |
| □y1h                                   |  |
| 🖂 transfac                             |  |
| de novo motif search                   |  |
| width of region to be scanned:         |  |
| 600                                    |  |
| p-value cutoff:                        |  |
| 0.001                                  |  |
| Execute                                |  |

- Search the sequence motifs around peak center positions
- Search in known motif databases
- Perform de novo motif discovery based on MDscan algorithm
- Cluster similar motifs



#### **Target Genes**

| Probe       | Symbol   | Description  | Gene        | Cytoband                      | Log2 ratio             | P.Value             |
|-------------|----------|--|-------------|-------------------------------|------------------------|---------------------|
| 200642 at   | SOD1     | superoxide dismutase 1,<br>soluble   | 6647        | 21q22.1<br>21q22.11           | 0.838190702613965      | 0.00802084649649879 |
| 200818_at   | ATP5O    | ATP synthase, H+<br>transporting, mitochondrial F1<br>complex, O subunit   | <u>539</u>  | 21q22.1-<br>q22.2<br>21q22.11 | 0.71181156889573       | 0.0063484296893304  |
| 201123 s at | EIF5A    | eukaryotic translation<br>initiation factor 5A                             | <u>1984</u> | 17p13-p12                     | -1.80077206732193      | 0.00802084649649879 |
| 201201 at   | CSTB     | cystatin B (stefin B)  | 1476        | 21q22.3                       | 0.686425433577363      | 0.0142335983540328  |
| 202217 at   | C21orf33 | chromosome 21 open reading<br>frame 33                                     | 8209        | 21q22.3                       | 0.595064830464679      | 0.00802084649649879 |
| 202325 s at | ATP5J    | ATP synthase, H+<br>transporting, mitochondrial F0<br>complex, subunit F6  | 522         | 21q21.1                       | 0.859556830155792      | 0.0135258116807050  |
| 206777 s at | CRYBB2   | crystallin, beta B2  | 1415        | 22q11.2-<br>q12.1<br>22q11.23 | -<br>0.805082151961259 | 0.00732899673114332 |
| 212269 s at | МСМЗАР   | minichromosome<br>maintenance complex<br>component 3 associated<br>protein | 8888        | 21q22.3                       | 0.616256113815303      | 0.0170513984158495  |
| 218386 x at | USP16    | ubiquitin specific peptidase 16  | 10600       | 21q22.11                      | 0.72435816091872       | 0.042867901131958   |
| 221677 s at | DONSON   | downstream neighbor of SON   | 29980       | 21q22.1                       | 0.59526907422616       | 0.0103108082416304  |









| Workflow Canvas   Generic ChIP-seq     |   |  |  |  |  |  |  |  |  |  |
|--|---|--|--|--|--|--|--|--|--|--|
|  |   |  |  |  |  |  |  |  |  |  |
| MACS 😫                                 | CEAS: Enrichment on chromosome and annotation       |  |  |  |  |  |  |  |  |  |
| Treatment file                         | > WIGGLE file<br>BED file(maximum 100000 lines)     |  |  |  |  |  |  |  |  |  |
| bedoutput (bed)<br>xlsoutput (tabular) | Gene List     Gene List     Gene List               |  |  |  |  |  |  |  |  |  |
| log (txt)                              | output (png)<br>log (txt)                           | ø<br>0   |  |  |  |  |  |  |  |  |
|  |   |  |  |  |  |  |  |  |  |  |
| Sort 💥                                 | Conservation / Aggregate D                          | atapoints 💥  |  |  |  |  |  |  |  |  |
| Sort Query                             | interval file 1 > Select another interval file      |  |  |  |  |  |  |  |  |  |
| out_file1                              | output (png)  |  |  |  |  |  |  |  |  |  |
|  | log (txt)   | 9  |  |  |  |  |  |  |  |  |
| Select first 🛛 🗱                       | Seqpos motif tool 🐰                                 | Seqpos motif tool 🛞                                      |  |  |  |  |  |  |  |  |
| from                                   | BED file (at most 10K                               | BED file (at most 10K                                    |  |  |  |  |  |  |  |  |
| out_file1                              | lines)  | lines)   |  |  |  |  |  |  |  |  |
|  | output_xml (xml)<br>output_html (html)<br>log (txt) | output_xml (xml)<br>output_html (html)<br>log (txt)<br>o |  |  |  |  |  |  |  |  |

## Future work

- More public ChIP-chip/seq datasets, precompiled in Cistrome DC.
- Correlation map of all avaiable data in DC.
- Integration. e.g. Galaxy->DC
  Follow Galaxy.

## Acknowledgement

#### • Cistrome Authors

- DFCI Team:
  - X. Shirley Liu, Myles Brown, Tao Liu, Cliff Meyer, Len Taing, Jian Ma, Meng Zhou, Ying Lei, Hyunjin Gene Shin, Yong Zhang
- Eli Lilly Team:
  - Yaron Turpaz, Jorge Cesar Andrade Ortiz, Teck Kwong Bernett Lee, Swee Seong Wong, Kar Joon Chew, Kevin Yeung Chung Pak, Michael Poidinger, Patrick Hartman
- Acknowledgement:
  - Yi Wang, Scott Taing, Jacqueline Wentz, Lingling Shen, Josiah Altschuler, Zeynep Coban, Wenbo Wang, Mayako Michino, Meng Zhou, Jeremy Wu, Hansen He, Yiwen Chen, Utz Pape, Bo Jiang, Xiangfeng Wang
  - Edmond Joseph Breen, Shan Ho Tan
  - Wei Li (Baylor), Jun Song (UCSF), Mathieu Lupien (Dartmouth)
  - Jason Lieb (UNC), Susan Strome (UCSC), Julie Ahringer (Cambridge), Mitchelle Lazar (UPENN), Christopher Glass (UCSD)