# **Encode Enhancer Challenge**

## Input Data

| file download from http://cistrome.org/db/#/     | ChIPTF          | GEO Accession Number        | Reference genome | tissue/cell ty |
|--|-----------------|-----------------------------|------------------|----------------|
| 54499_H3K27ac_sort_peaks.narrowPeak.gz           | H3K27ac         | GSM851284                   | mm10             | Embryonic I    |
| $5060\_OLIG2\_sort\_peaks.narrowPeak.gz$         | OLIG2           | GSM766058                   | mm10             | Embryo         |
| $60947\_H3K4me2\_sort\_peaks.narrowPeak.gz$      | H3K4me2         | GSM632045                   | mm10             | Embryo         |
| $55119\_SOX2\_sort\_peaks.narrowPeak.gz$         | SOX2            | GSM1033096                  | mm10             | Embryo         |
| $62993\_H3K27ac\_sort\_peaks.narrowPeak.gz$      | H3K27ac         | GSM1264370                  | mm10             | Heart          |
| $68244\_H3K4me1\_Ren\_sort\_peaks.narrowPeak.gz$ | H3K4ME1_E14.5   | GSM1000136                  | mm10             | Heart          |
| $56691\_POLII\_sort\_peaks.narrowPeak.gz$        | POLR2A          | GSM1163129                  | mm10             | Cardiomyoc     |
| $68115\_EP300\_Ren\_sort\_peaks.narrowPeak.gz$   | P300_ADULT-8WKS | GSM918747                   | mm10             | Heart          |
| $53322\_H3K4me1\_sort\_peaks.narrowPeak.gz$      | H3K4me1         | GSM851281                   | mm10             | Embryonic I    |
| $5097\_HOXC9\_sort\_peaks.narrowPeak.gz$         | HOXC9           | GSM766061                   | mm10             | Embryo         |
| $54562\_H3K27ac\_sort\_peaks.narrowPeak.gz$      | H3K27ac         | $\operatorname{GSM1039565}$ | mm10             | Hindlimb Au    |
| $58262\_SPI1\_sort\_peaks.narrowPeak.gz$         | SPI1            | GSM878650                   | hg38             | Fetal Brain    |
| $1491 \_DNase\_sort\_peaks.narrowPeak.gz$        | DNase           | GSM595926                   | hg38             | Fetal Brain    |
| $1932\_{\rm EP300\_sort\_peaks.narrowPeak.gz}$   | EP300           | GSM602299                   | hg38             | Neuroectode    |
| $53421\_H3K4me1\_sort\_peaks.narrowPeak.gz$      | H3K4me1         | GSM772785                   | hg38             | Neuron         |
| $61864\_H3K27ac\_sort\_peaks.narrowPeak.gz$      | H3K27ac         | $\operatorname{GSM956008}$  | hg38             | Embryo         |
| $54525\_H3K27ac\_sort\_peaks.narrowPeak.gz$      | H3K27ac         | $\operatorname{GSM}910557$  | hg38             | Right Atriur   |
| $58256\_SPI1\_sort\_peaks.narrowPeak.gz$         | SPI1            | GSM878630                   | hg38             | Fetal Heart    |
| $1545\_DNase\_sort\_peaks.narrowPeak.gz$         | DNase           | GSM665811                   | hg38             | Fetal Heart    |
| $61702\_H3K9ac\_sort\_peaks.narrowPeak.gz$       | H3K9ac          | GSM706849                   | hg38             | Heart          |
| $58318 \_DNase\_sort\_peaks.narrowPeak.gz$       | DNase           | GSM1027324                  | hg38             | Fetal Renal    |
| 58242_SPI1_sort_peaks.narrowPeak.gz              | SPI1            | GSM878662                   | hg38             | Fetal Renal    |
|  |                 |                             |                  |                |

### Method 1(using ChIPseq signal as features)

- Select relative ChIPseq dataset based on Enrichment in VISTA regions and prior knowledge
- Liftover hg19 coordinates of VISTA regions to hg38 and mm9 coordinates of VISTA regions to mm10
- Annotate VISTA region with overlaping ChIP-seq dataset peak score. At this step, hg38 regions associate with scores only from hg38 chipseq peaks, and similarly mm10 regions only associate with mm10 chipseq peak
- Annotate regions highly conversed across human and mouse with both peaks score from two species. Highly conserved regions are defined based on UCSC liftOver 0.95 conserved At this step, we have a feature matrix with missing values: each row is VISTA region and each column is one ChIP-seq signal feature for both mm10 and hg38
- Impute the missing value using R package "mi"
- Train 3 binary classification problems based on the imputed feature matrix and label of each VISTA region: brain, heart, other enhancer
- Build logistic regression model using R package "glmnet"
- Predict LBNL tested regions: construct imputed feature matrix for tested regions as stated above, apply the trained logistic model to predict the probability of each types of enhancer in the given tested regions.
- Predict genome-wide regions: construct imputed feature matrix for human DHS region with GWAS SNPs, apply the train model above to predict three probabilities for each region, finally convert coordinate to mm10

#### output files:

- 240 LBNL test regions prediction: PredictionUsingChIPSeq.txt
- Regions likely to function in e11.5 mouse embryo: GenomeWide5kPredictionUsingChIPSeq.txt

## Method 2(using Kmer frequency as features)

- Two types of Kmer features are used: 8mer frequency allowing 3 mismatches , 5mer pair allow 1 mismatch and 0-30bp gap in between two 5mers
- Train: for each VISTA region sequence, extract Kmer frequency vector, build logistic regression model using R package "glmnet" for 3 enhancer classification problems: brain, heart, other enhancer
- Predict LBNL tested regions: extract Kmer frequency feature vector for each test regions, and apply the trained logistic model to predict the probability of each types of enhancer in the given tested regions
- Prioritize other genomics regions: only use top5k regions predicted by chipseq feature method, and apply the trained logistic model(Kmer model) to predict the probability of each types of enhancer in the given 5k regions, and report the predictive probability of those highly positive regions.

#### output files:

- 240 LBNL test regions prediction: PredictionUsingKmer.txt
- Regions likely to function in e11.5 mouse embryo: GenomeWide5kPredictionUsingKmer.txt

### output file format:

- first row: indication of types of enhancer for last 3 columns
- column 1:mm10 coordinates of predicting region
- column 2: probability of the given region is a enhancer in any tissue of e11.5 mouse
- column 3: probability of the given region is a enhancer in forebrain tissue of e11.5 mouse
- column 4: probability of the given region is a enhancer in heart tissue of e11.5 mouse

#### Submission Files

- Under submission folder, there are two sets of files: set1\_xxx(prediction from method1) and set2\_xxx(prediction from method2)
- setX file1,2,3,4: follow the order of submission guideline:
  - File 1 of prediction corresponding to heart regions being tested (120 regions) bed5 format: first 3 columns correspond to chromosome, start, end of prediction. 4th column is prediction probability of being active in heart, 5th column is prediction probability of being active in any tissue.
  - File 2 of prediction corresponding to forebrain regions being tested (120 regions) bed5 format: first 3 columns correspond to chromosome, start, end of prediction. 4th column is prediction probability of being active in forebrain, 5th column is prediction probability of being active in any tissue.
  - File 3 of prediction genome-wide heart predictions (<= 5k regions) bed4 format : first 3 columns correspond to chromosome, start, end of prediction. 4th column is prediction probability of being active in heart.
  - File 4 of prediction genome-wide forebrain predictions (<= 5k regions) bed4 format : first 3 columns correspond to chromosome, start, end of prediction. 4th column is prediction probability of being active in forebrain.