ChIP-Seq (chromatin immunoprecipitation sequencing) is a method to sequence the DNA fragments that co-precipitate with proteins. ChIP Seq assays have become an indispensable next generation technique for detecting in vivo interactions of DNA target sites against their corresponding transcription factors (TFs), epigenetic histone modifications, as well as chromatin remodeling. Transcription factor ChIP-Seq helps one create genome wide profiling of the precise regulatory sites of a transcription factor (TF) in a genome. ChIP-Seq data is traditionally analyzed to recognize enriched motifs that are enriched for a TF or study gene ontology relationships. In more recent studies, ChIP-Seq data is studied in close integration with forms of sequencing data like RNA-Seq, ATAC-Seq, etc.

RNA-Seq is mostly used to analyze quantitative difference in expression of the genes across various conditions. A plethora of tools have been devised to construct a list of differentially expressed genes accurately. Having the quantitative information enables bioinformaticians to visualize the data using heatmaps, volcano plots, PCR plots and conduct pathway enrichment studies.

The abundance of data pertaining to RNA-Seq and ChIP-Seq paves way for integration of these two sequencing technologies. Combining these complimentary approaches may serve to fill the gaps and overcomes the challenges posed by these two methods. Data from ChIP-Seq can strengthen data generated from RNA-Seq and helps researchers decipher the underlying gene regulation mechanisms, thereby enhancing our understanding of the genome. Consolidation of RNA-Seq and ChIP-Seq allows the detection of the most enriched transcription factor in the differentially expressed genes, and these DEGs could be direct targets of the enriched factors.

ChuRN is novel, easy to use application that allows the user to enter RNA-Seq data and choose the transcription factor he wants to analyze. CHuRN takes the counts matrix and metadata files (RNA-Seq) of an experiment as an input. The application allows the user to enter the transcription factor and cell line desired for integrative analysis. In the backend, the application uses the read counts to generate a list differentially expressed genes using DeSeq2. The app extracts the peak file of the desired TF and cell line from the ENCODE repository. As a final step, the list of DEGs and the peak file information is used by a tool named BETA. BETA finally gives a text output file (with a graphical output) which has the list of upregulated and downregulated target genes for the desired transcription factor.

Tools used by CHuRN

1. BETA
2. DeSeq2

Inputs required:

1. Read counts matrix (.txt, .tsv or .csv)
2. Metadata file (.tsv)
3. Choosing the TF factor and cell line from the dropdown menu

Output formats

1. List of upregulated and downregulated genes (.txt) output files generated by BETA

Citations:

1. Wang, S., Sun, H., Ma, J., Zang, C., Wang, C., Wang, J., ... & Liu, X. S. (2013). Target analysis by integration of transcriptome and ChIP-seq data with BETA. ***Nature protocols***, 8(12), 2502-2515.
2. Love MI, Huber W, Anders S (2014). “Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2.” Genome Biology, **15**, 550. doi: [10.1186/s13059-014-0550-8](https://doi.org/10.1186/s13059-014-0550-8).