Handout for part III of the EpiGenome Browser Workshop

0. Introduction

We will demonstrate how to make epigenetic annotation to noncoding SNPs using the Roadmap EpiGenome Browser (http://epigenomegateway.wustl.edu/browser/roadmap). The Roadmap Browser is based on the WashU EpiGenome Browser and has dedicated functions for accessing and analyzing huge volume of epigenomics information.

1. Launching the Roadmap EpiGenome Browser

- Choose reference genome
- Choose view range
- Choose epigenetic mark

- RECOVER session: H3K4me3 profile over default region in the human genome
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/2105449020.json

2. Navigating the Roadmap EpiGenome Browser

- Position the browser to the promoter region of *CHRNA7* gene in the human genome.
- Compare the H3K4me3 profiles (marking accessible gene promoters) of many human samples over the *CHRNA7* gene promoter region, especially for brain and blood samples, based on hierarchical data clustering analysis.
- Add H3K27me3 mark (marking repressive chromatins) and compare both histone marks over the *CHRNA7* gene promoter in the same set of samples.

- RECOVER session: covariation of H3K4me3 and H3K27me3 over *CHRNA7* gene promoter in the human genome
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/569628616.json

3. Epigenetic annotation of a noncoding SNP

- rs756699, located at chr5, 133446575 of the human hg19 genome. Found to be associated with multiple sclerosis by GWAS (Sawcer S. Nature, 2011)
- Show H3K4me1 profiles (marking enhancers) over a 5 kb region surrounding this SNP. Observe that the SNP is located in strong H3K4me1 modified-region specifically in blood cells.

- RECOVER session: H3K4me1 profile over 10 kb region surrounding SNP rs756699
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/937810367.json

- Show RNA-seq profile for a nearby gene *TCF7*, and observe the co-occurrence of H3K4me1 profile and high expression of *TCF7* gene in blood cells, suggesting a potential regulatory relationship between the enhancer and *TCF7*.
- Conclusion: this SNP is co-localizing with a potential blood-specific enhancer and may contribute to the disruption of *TCF7* gene expression.

- RECOVER session: covariation of H3K4me1 profile over the SNP, and RNA-seq profile for *TCF7* gene
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/1981500908.json

- Parallel display of the H3K4me1 profiles of many SNPs, by running gene set view on following SNPs. Remember to select 5 kb region surrounding each SNP:

chr1	10353111	10353112	rs10492972
chr1	85772008	85772009	rs233100
chr1	93303602	93303603	rs6604026
chr1	101331535	101331536	rs12048904
chr1	101407518	101407519	rs11581062
chr1	117038286	117038287	rs12025416
chr1	117100956	117100957	rs1335532
chr1	117104214	117104215	rs2300747
chr1	179469313	179469314	rs12047808
chr10	6099044	6099045	rs2104286
chr10	6102011	6102012	rs12722489
chr10	6110828	6110829	rs7090512
chr10	43814048	43814049	rs2503875
chr10	81036006	81036007	rs1250540

- RECOVER session: H3K4me1 profile over 14 SNPs
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/681261629.json

4. Human-mouse epigenome comparison

- Restart the browser, choose both hg19 and mm9 genomes.
- At the view range selection step, choose a new region for hg19, a homologous region will be automatically shown for mm9. Vice versa.
- Launch the browser to display human and mouse epigenomes in parallel fashion. Use a menu function to keep homology relationship between the human and mouse browser panels, e.g. to show orthologous genes.

- RECOVER session: human and mouse H3K4me3 profile comparison across *CHRNA7* gene promoter region
  http://epigenomegateway.wustl.edu/browser/roadmap/?pin=http://epigenomegateway.wustl.edu/browser/roadmap/t/618811412.json