

Capstone 2:

Adult and Disease Epigenetic Map

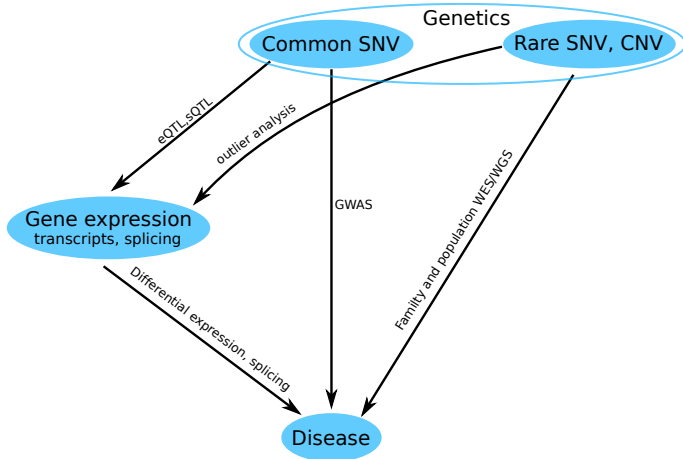
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Icahn School of Medicine at Mount Sinai

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University of Massachusetts Medical School

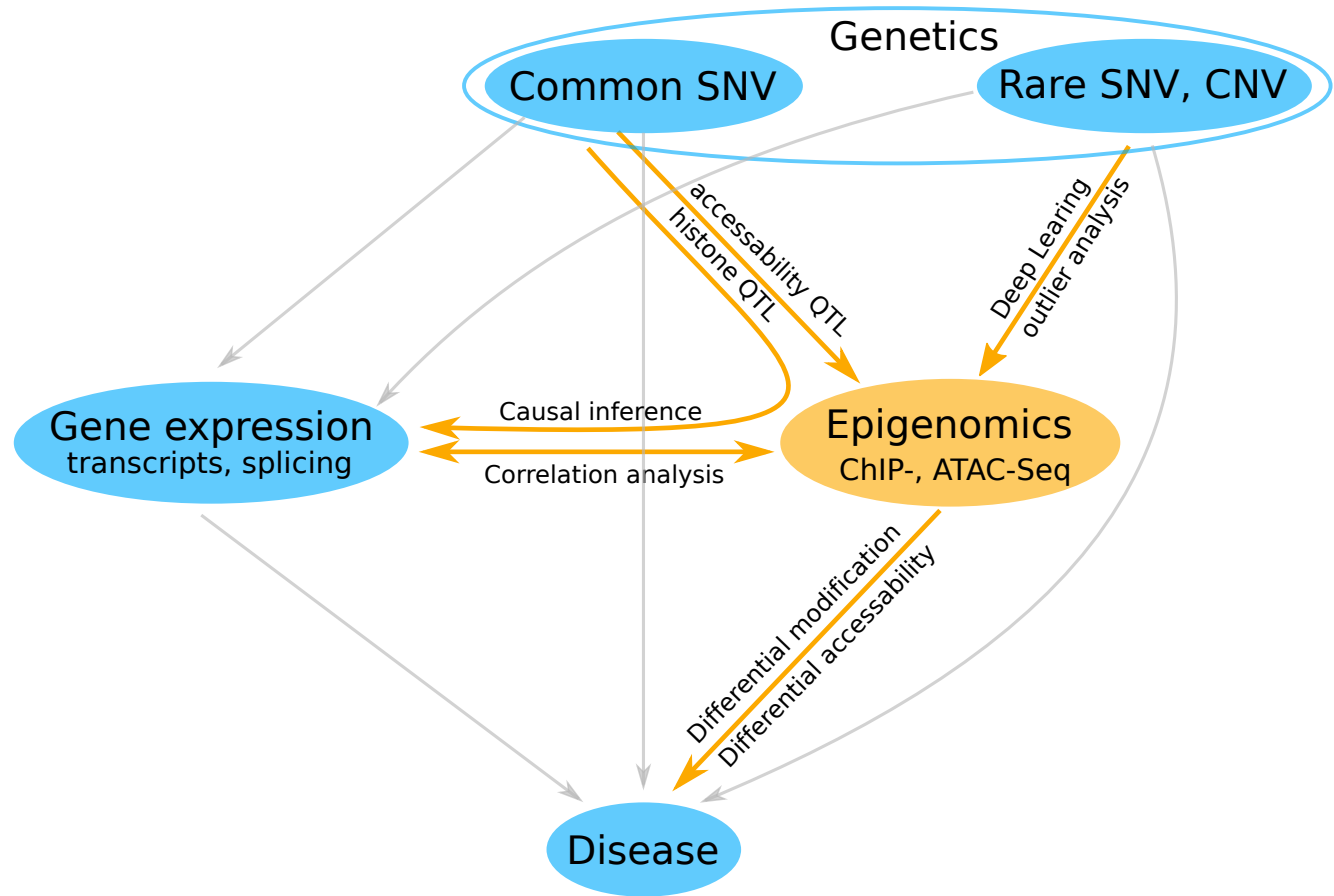
October 27, 2017

Foundation for Integrative Psychiatric Genomics

Current State of Psychiatric Genomics



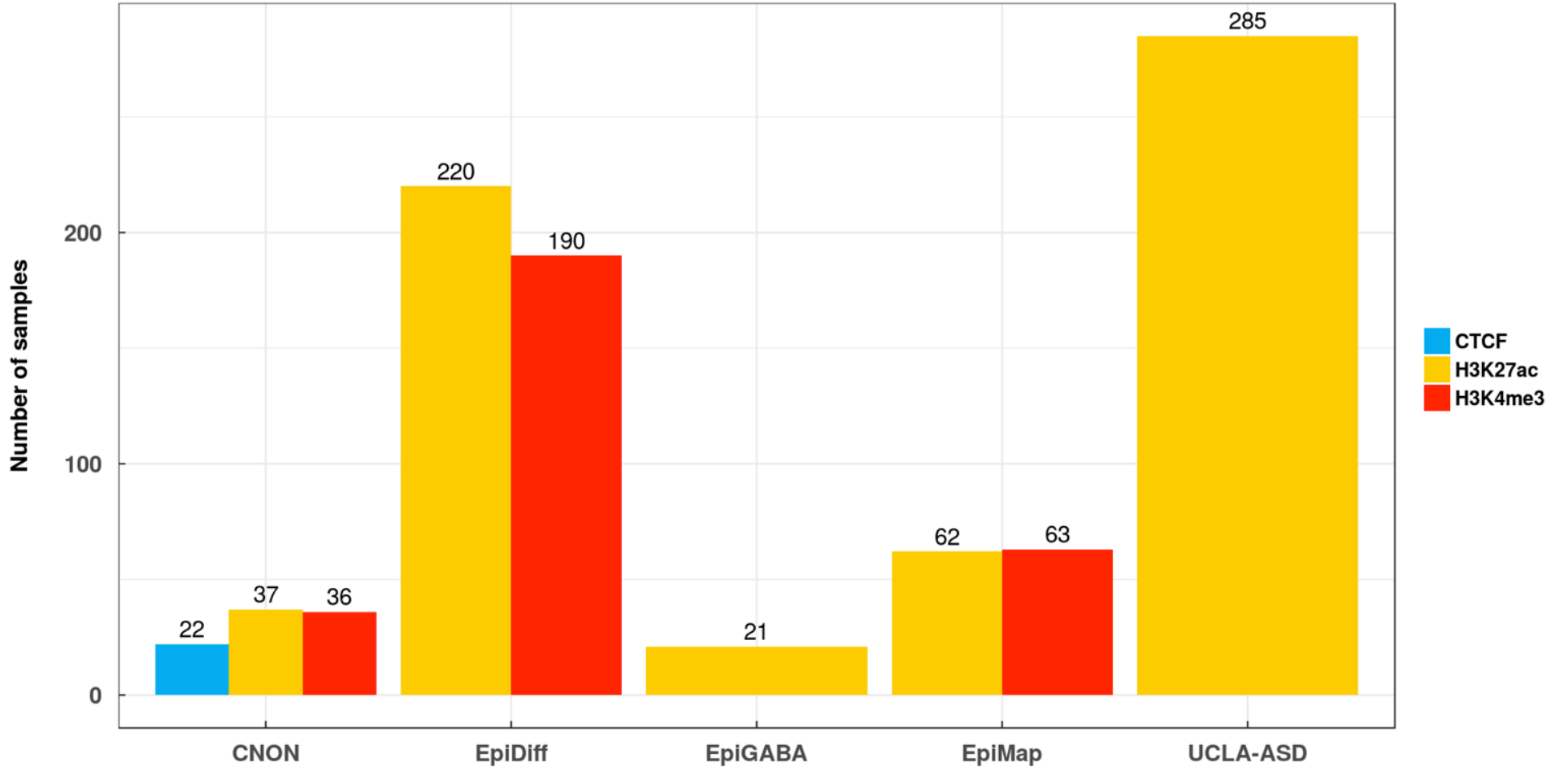
Next Generation Psychiatric Genomics



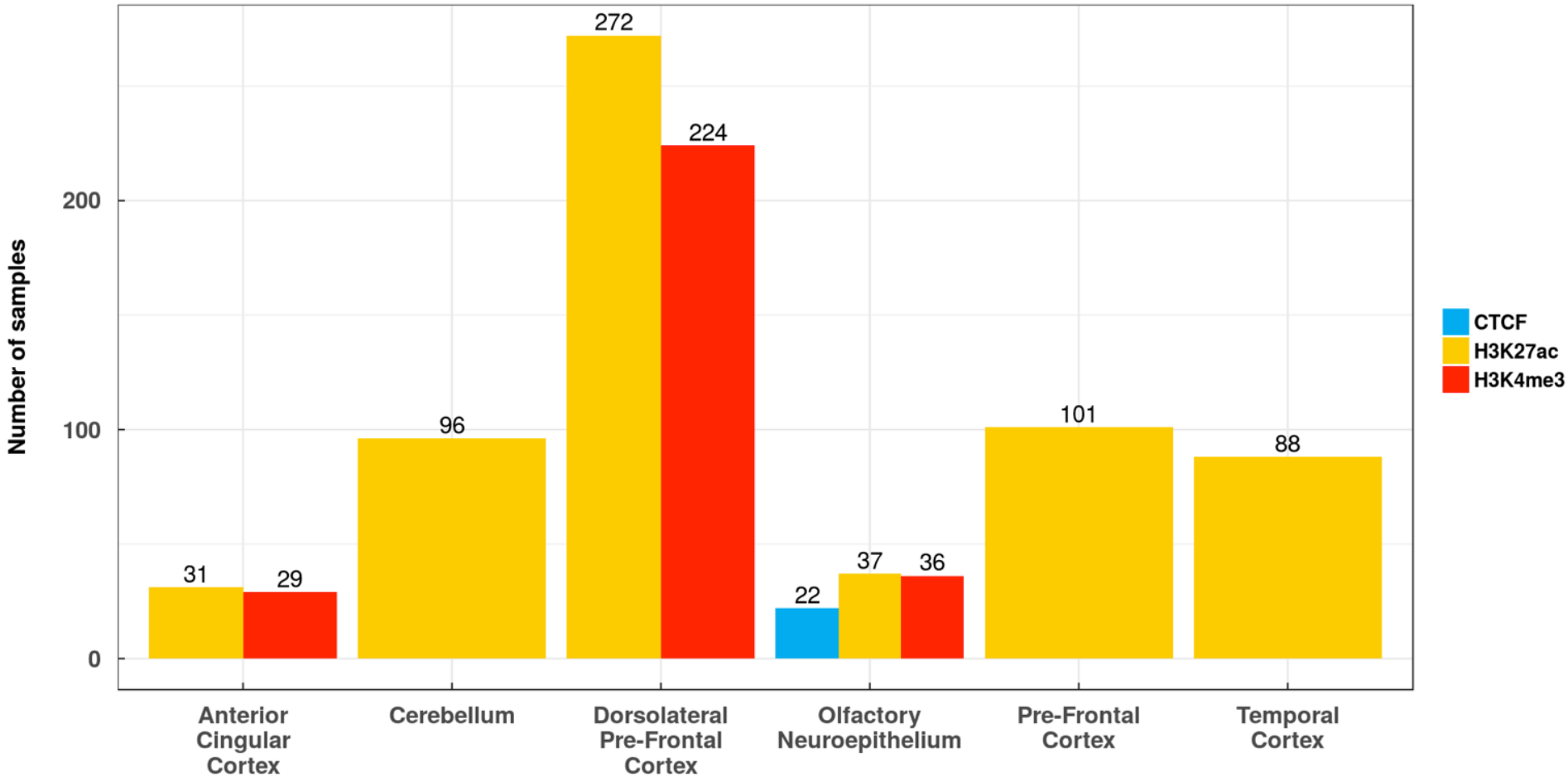
Analysis Goals

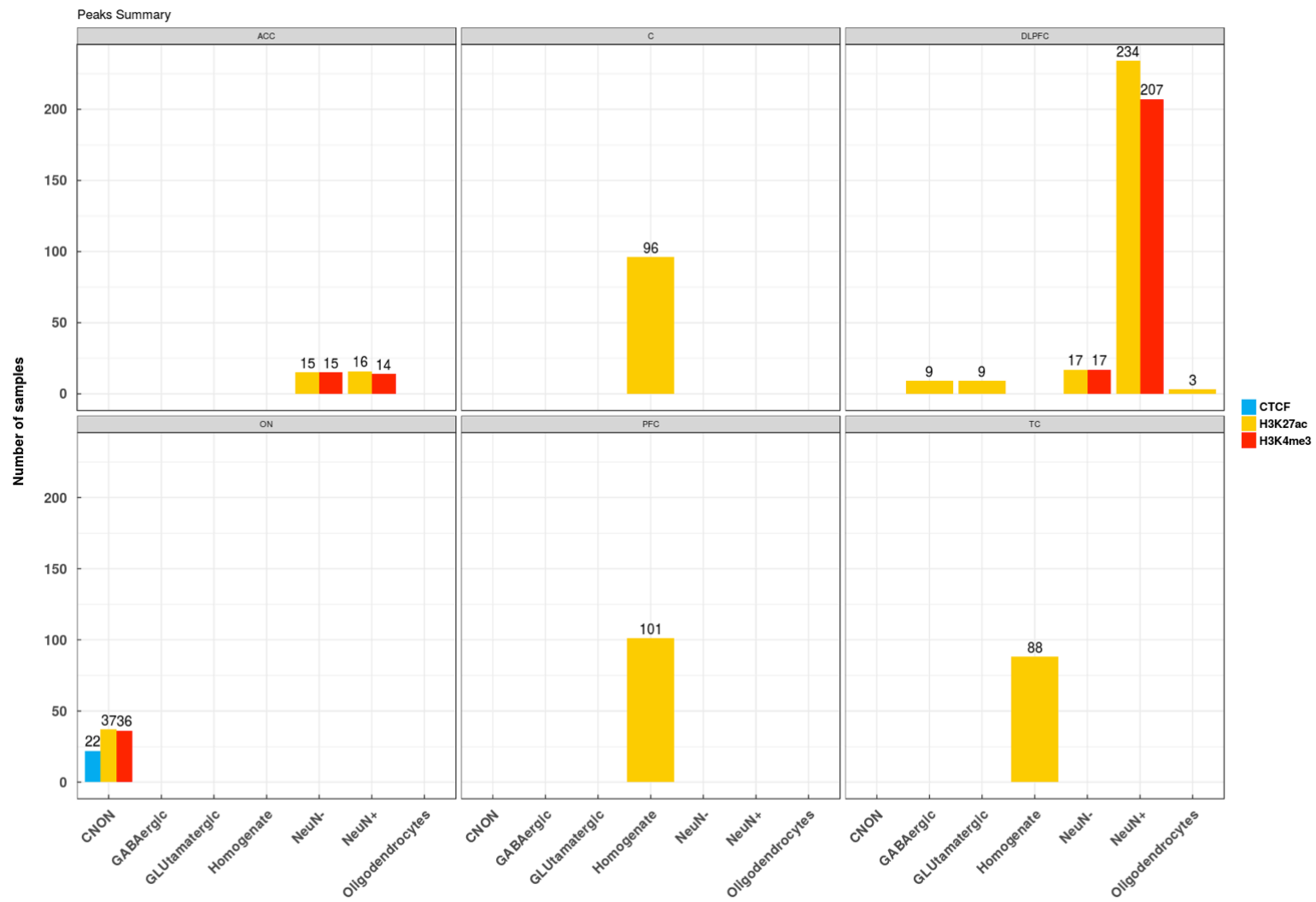
- Uniform data processing, finalize QC
- Differential modification analysis between cell types and brain regions
- Role of cell type composition in epigenetic variation
- Genetic regulation of histone modification
 - integrate with GWAS and eQTL summary statistics
- Interpret the effect of non-coding variation

Number of Samples Per Study

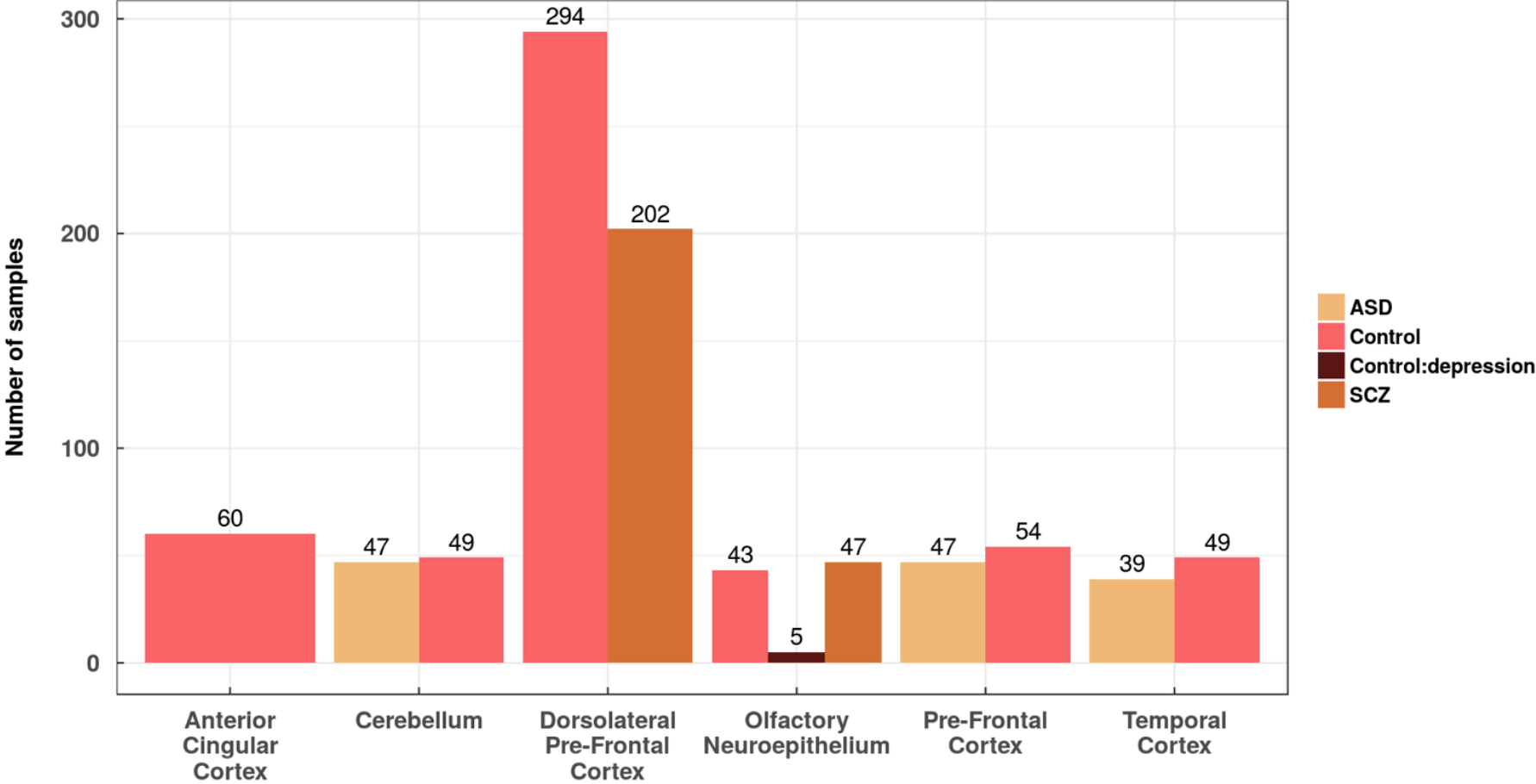


Number of Samples Per Brain Region

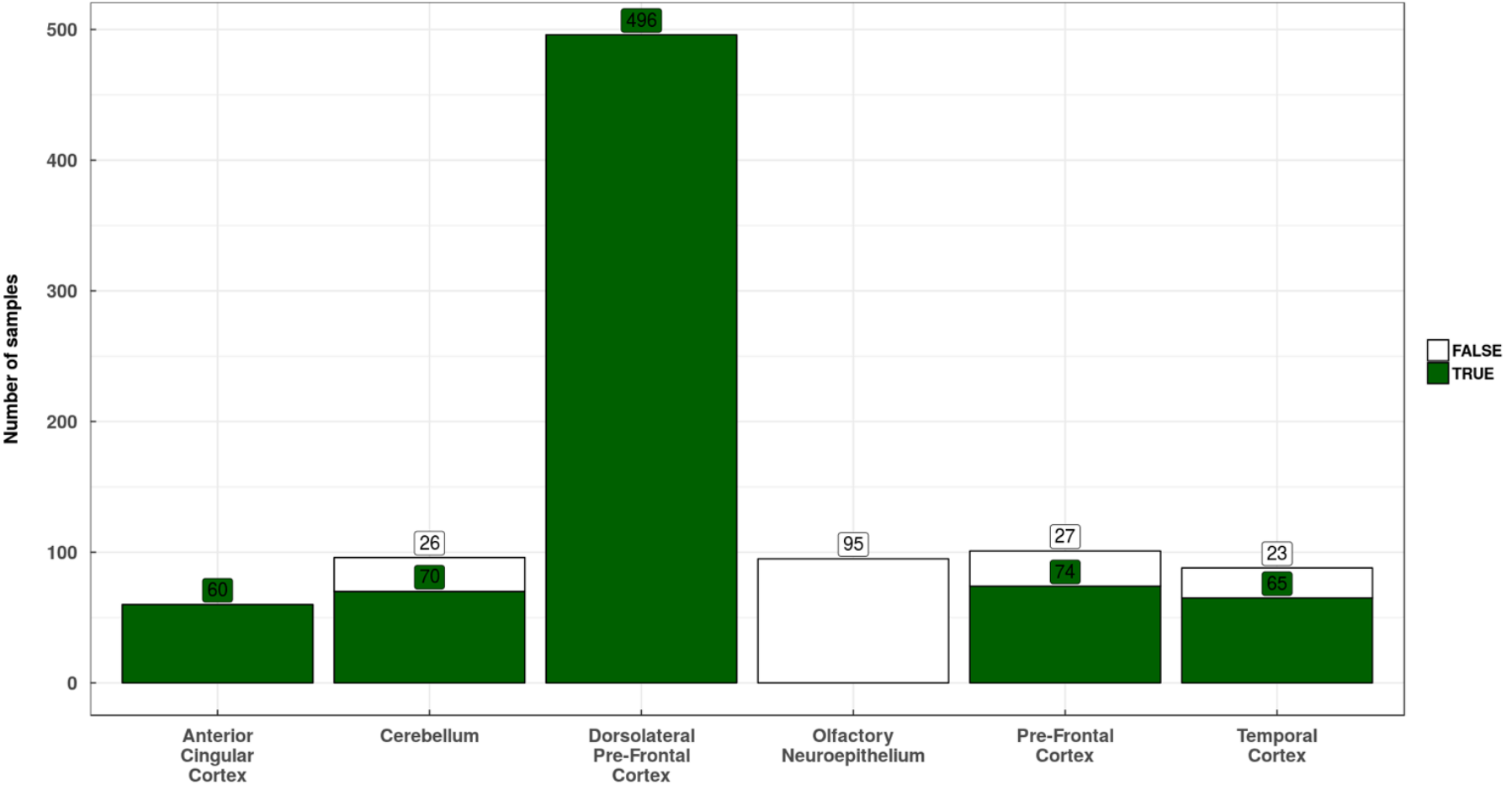




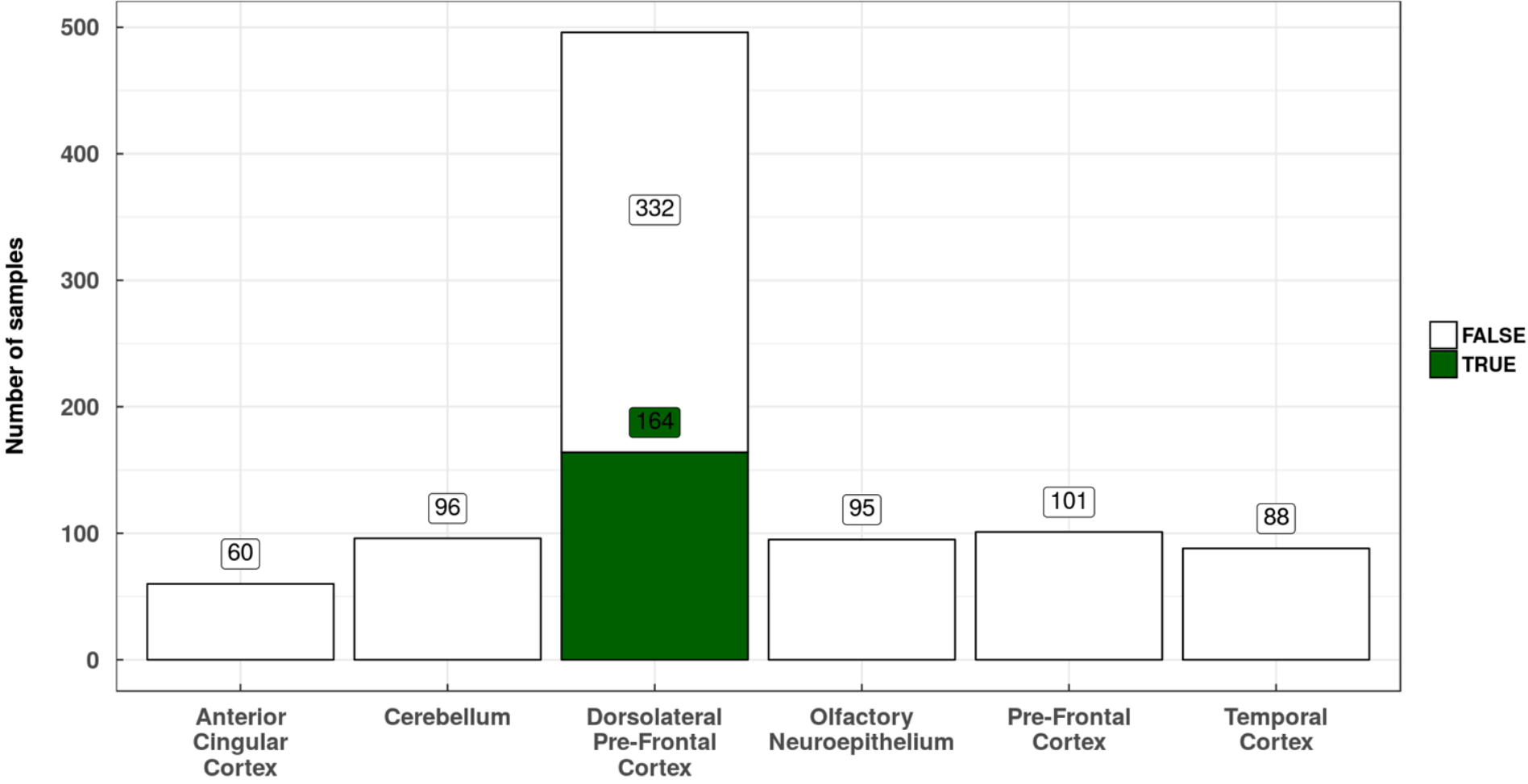
Number of Samples Per Diagnosis



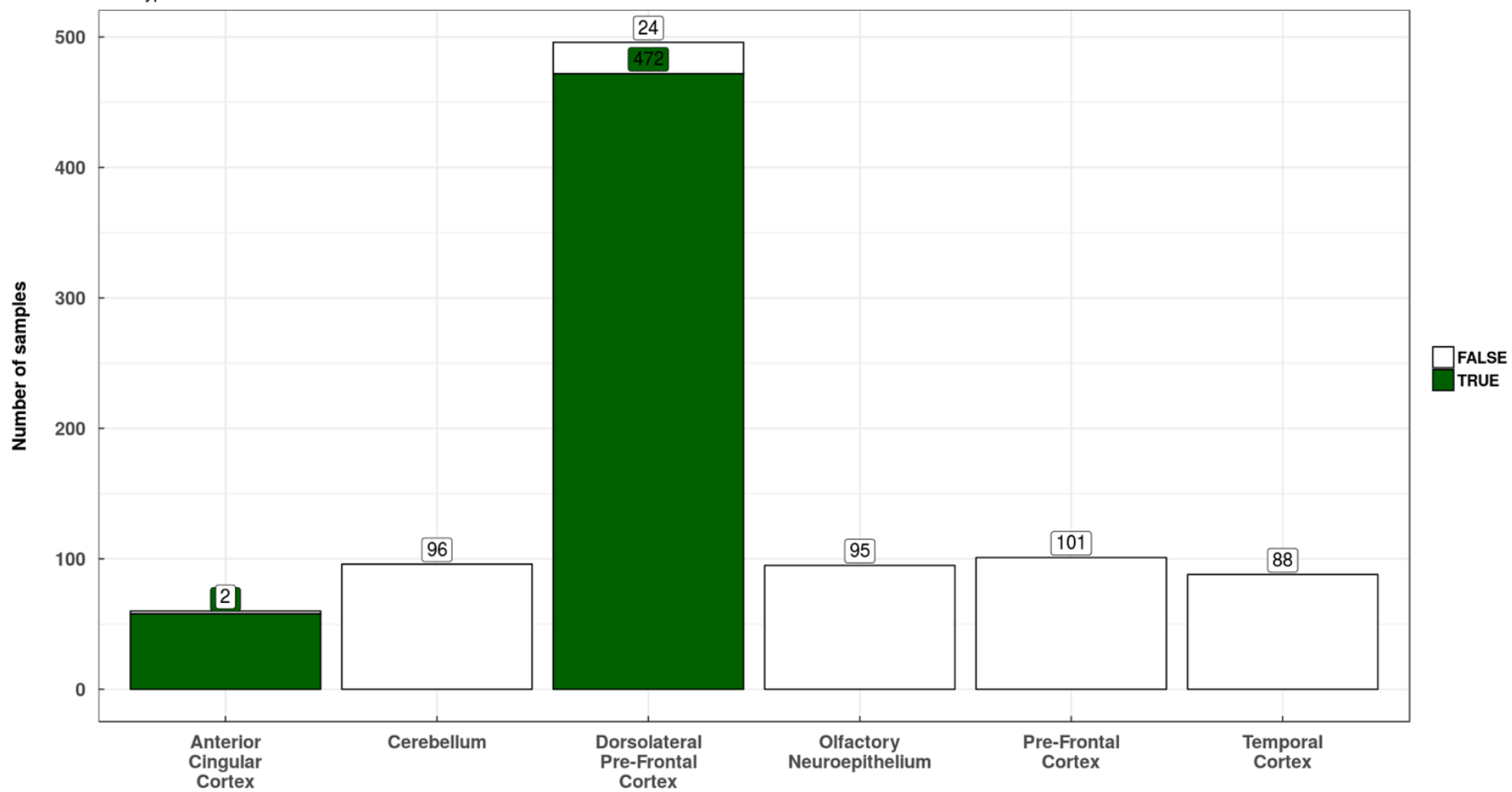
RNAseq Statistics



ATACseq Statistics



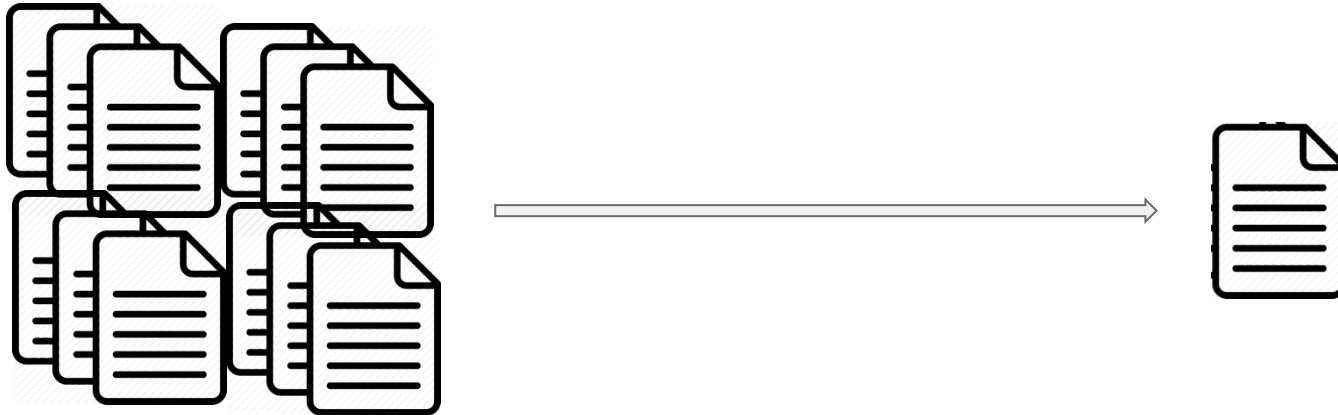
Genotype Statistics



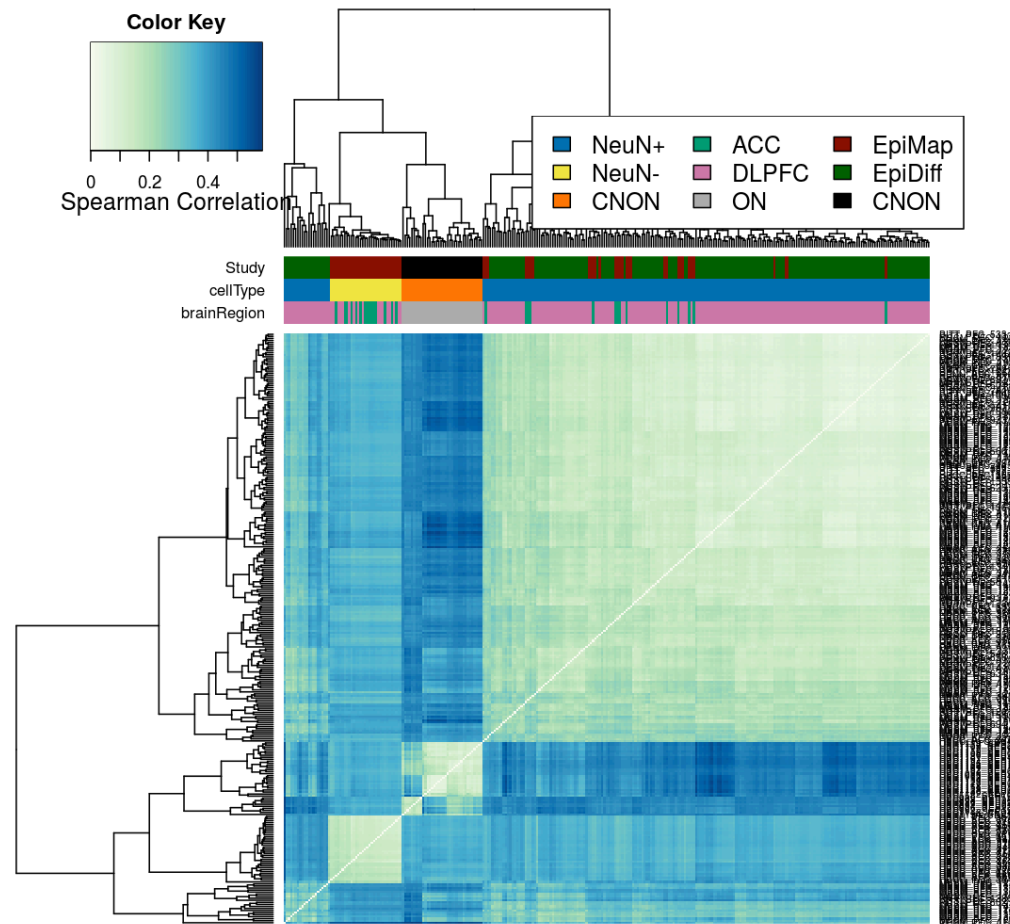
Create a consensus peak for H3K4me3

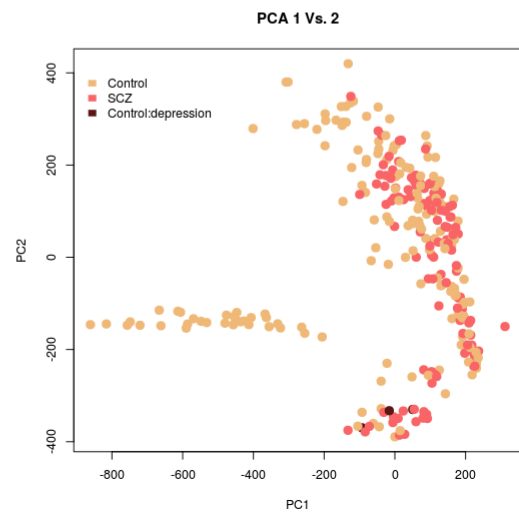
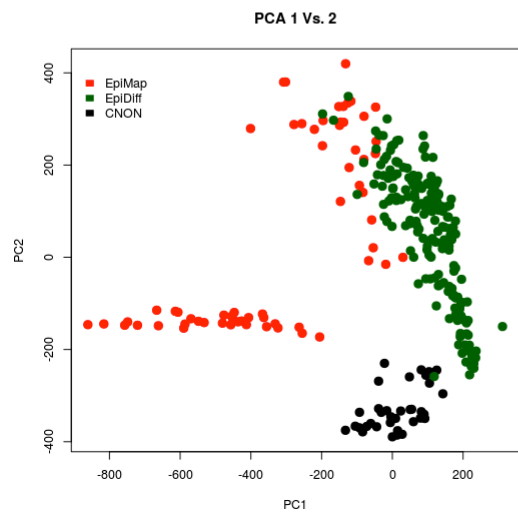
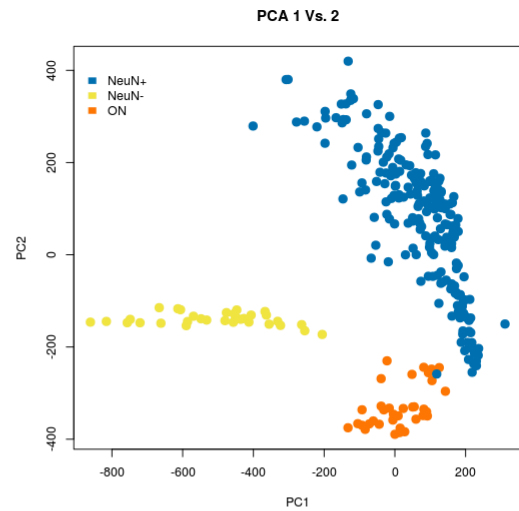
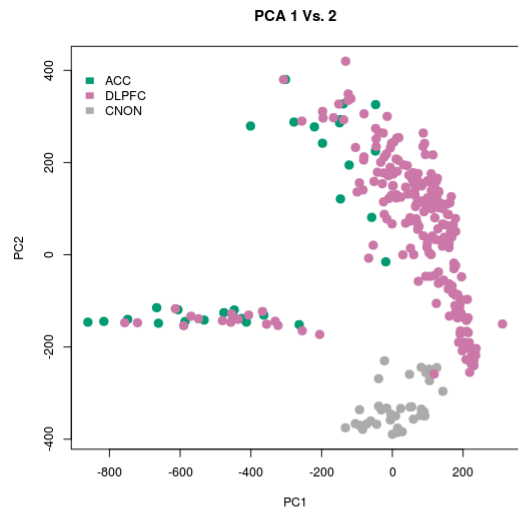
Merge all the narrow peaks

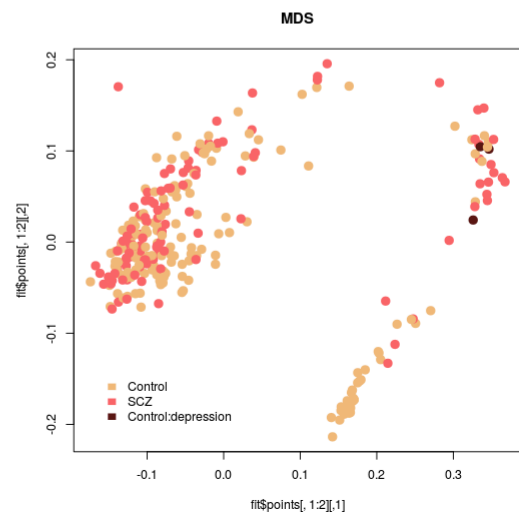
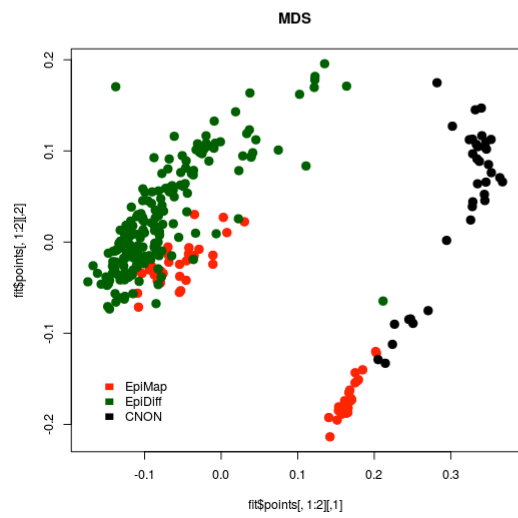
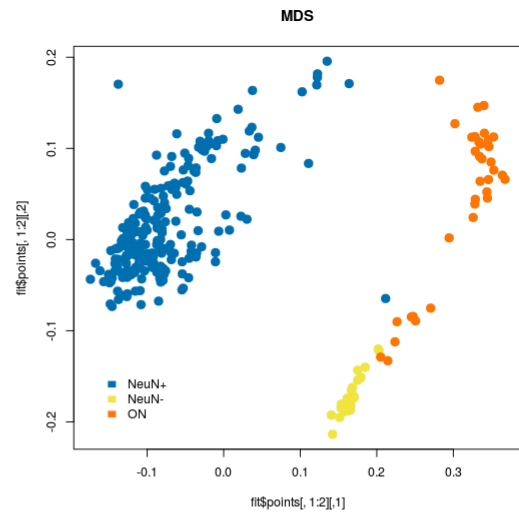
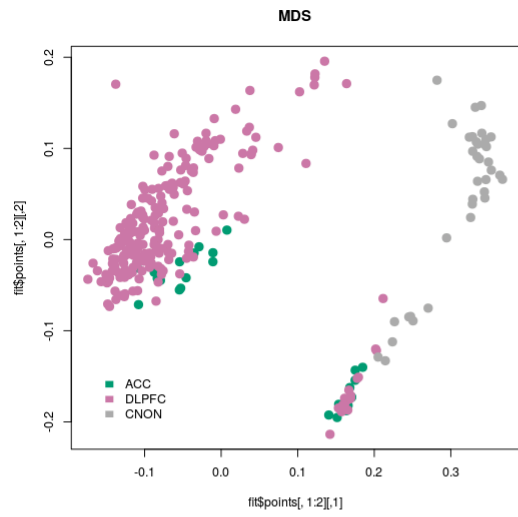
Consensus Peaks



Keep all the peaks
where at least in one
Study, 10% of
individuals show
significant coverage
(cpm>1)



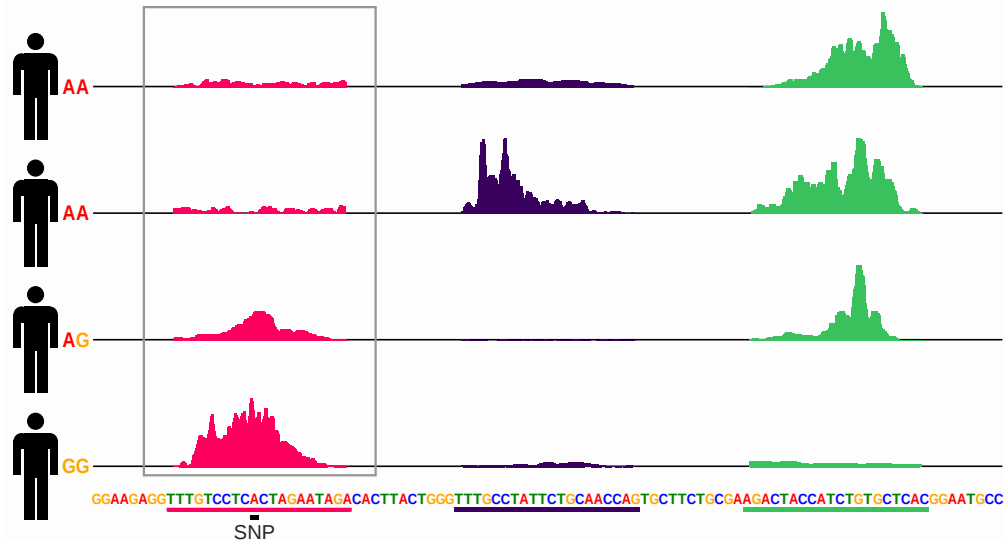




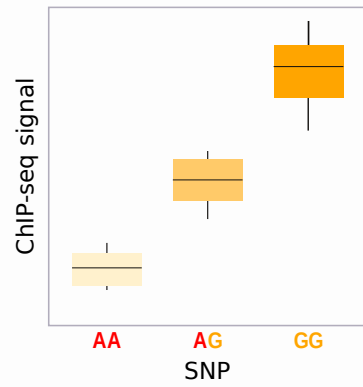
Genetics-only approach

histone QTL

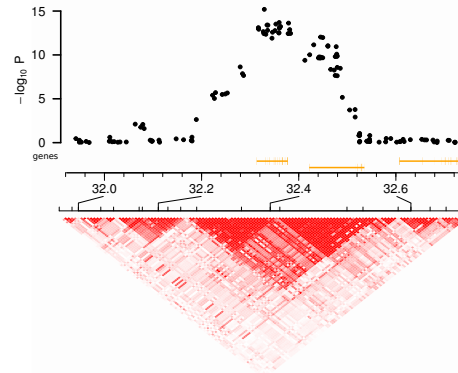
ChIP-seq for multiple subjects



hQTL



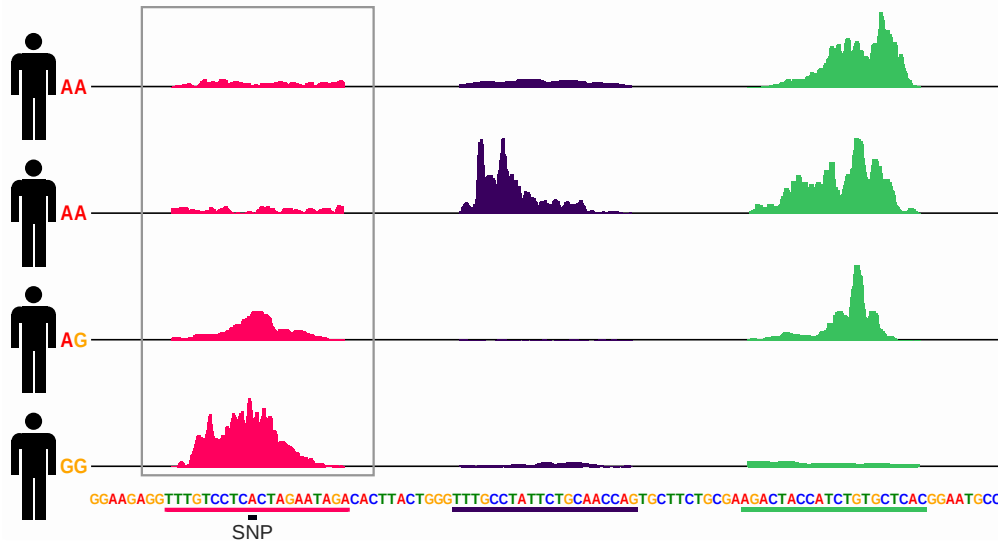
Linkage disequilibrium



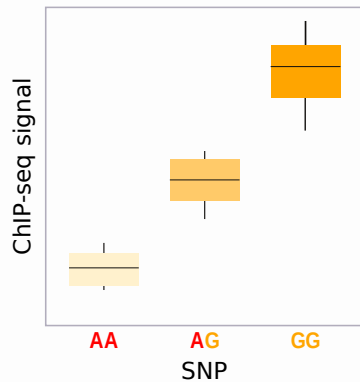
Neural network functional prediction

histone QTL

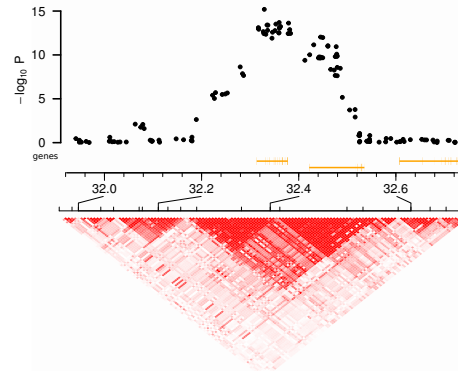
ChIP-seq for multiple subjects



hQTL

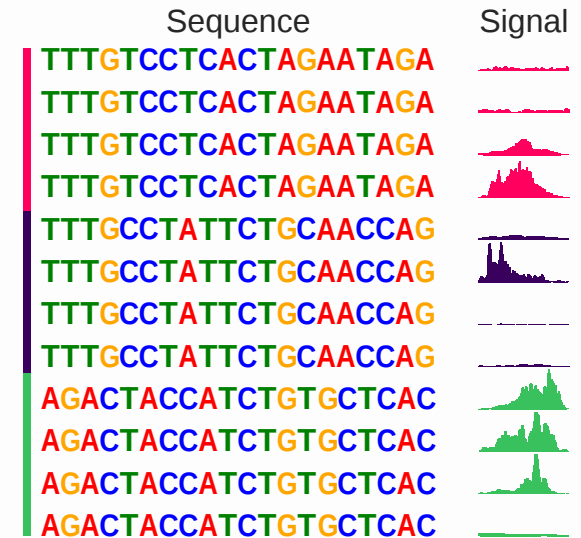


Linkage disequilibrium

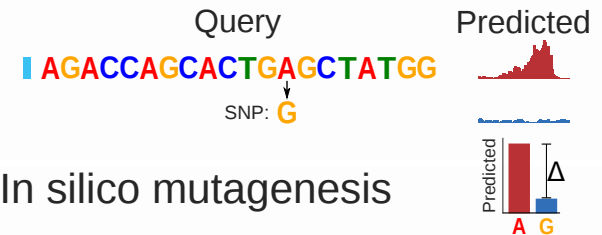


Convolutional neural network (CNN) prediction

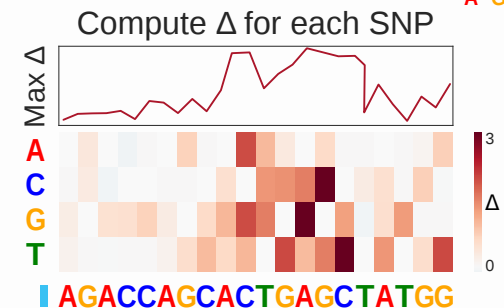
Train CNN



Prediction



In silico mutagenesis



Neural network functional prediction

Data

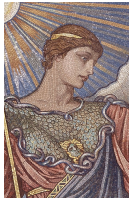
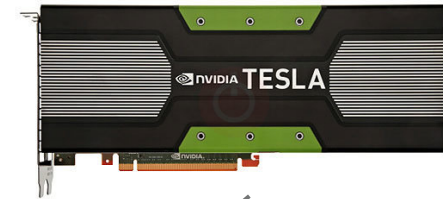


Software



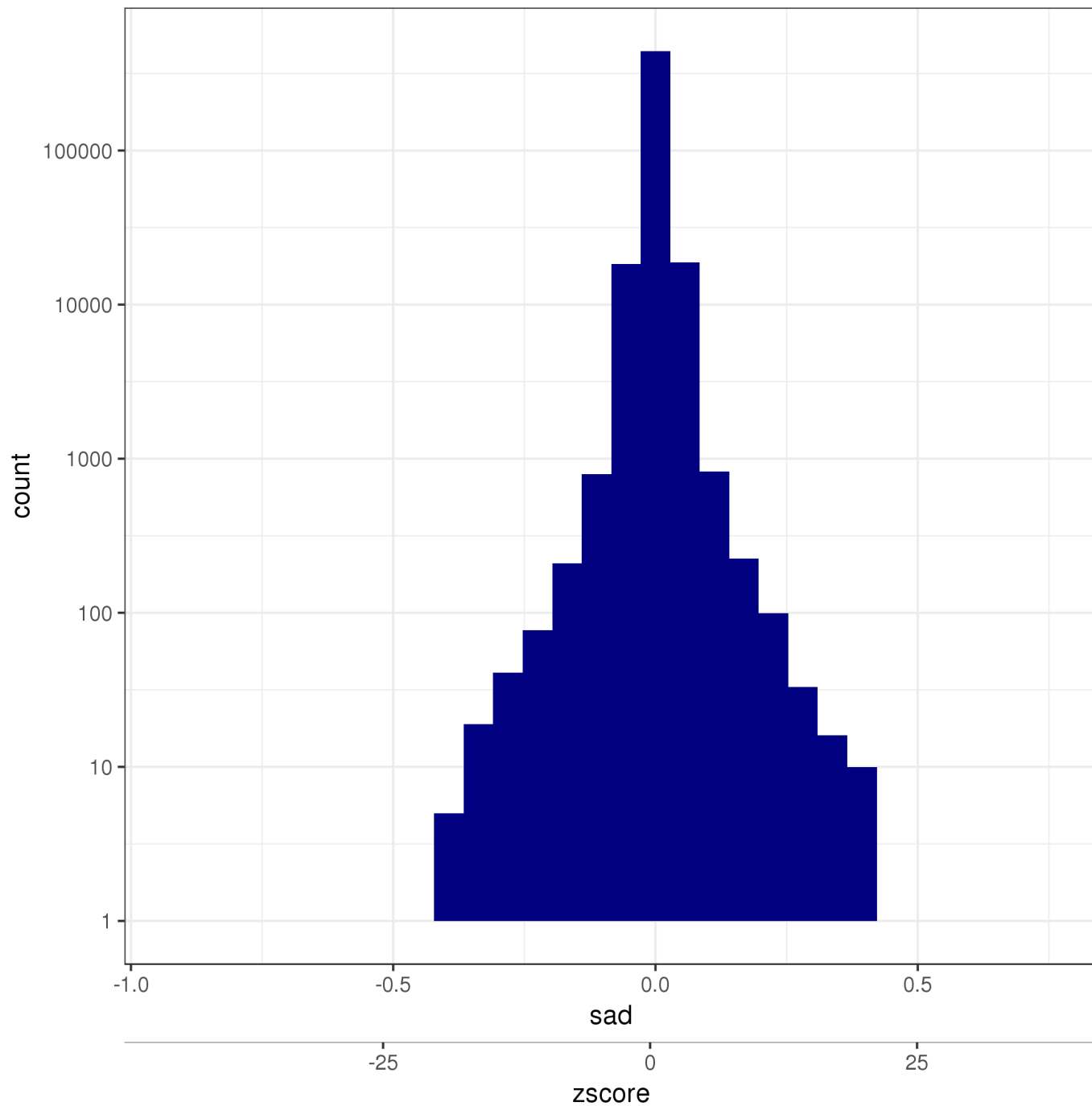
Basset (Kelly, et al. 2016, Genome Research)

Hardware

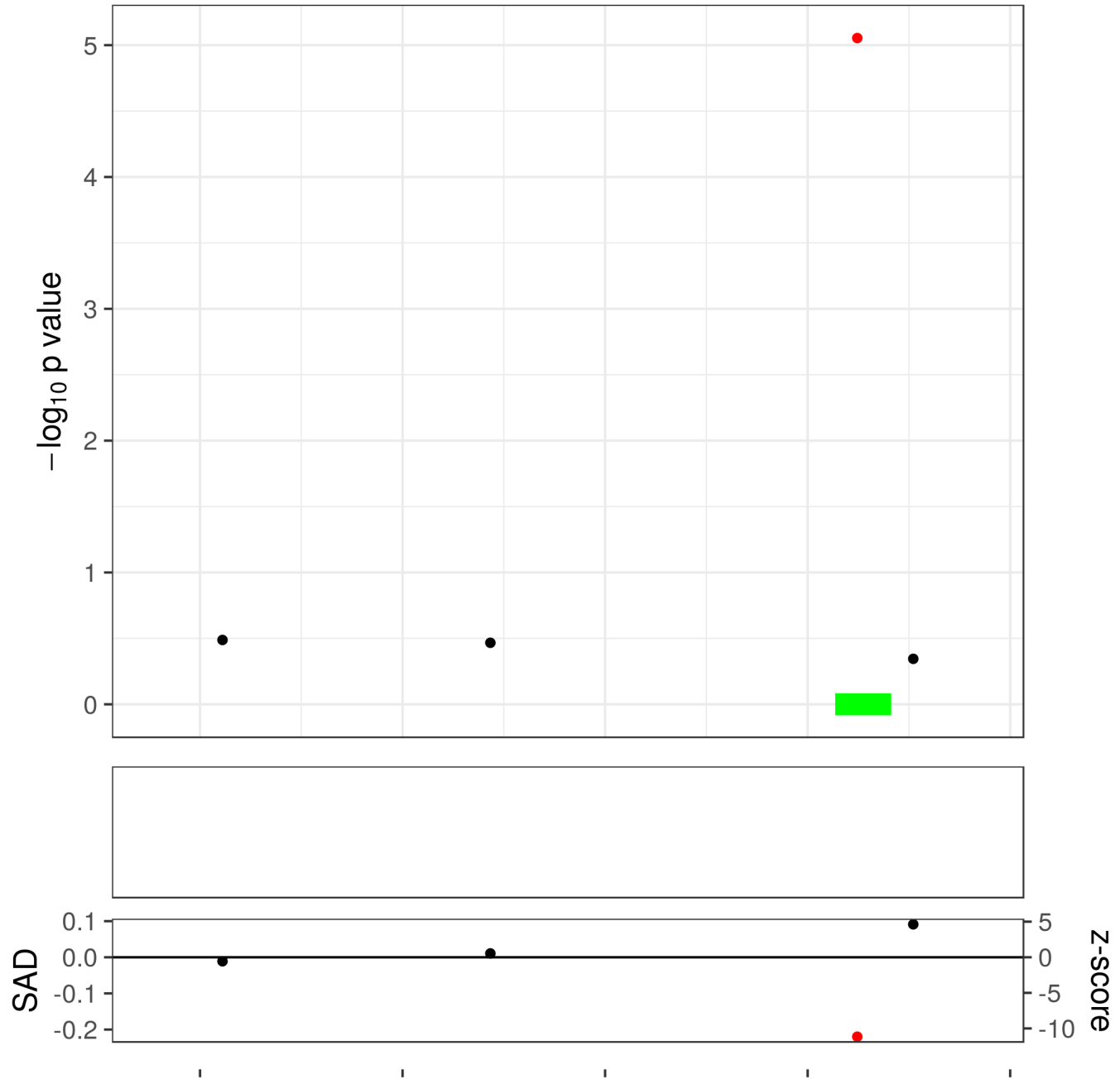


Variant-level functional prediction

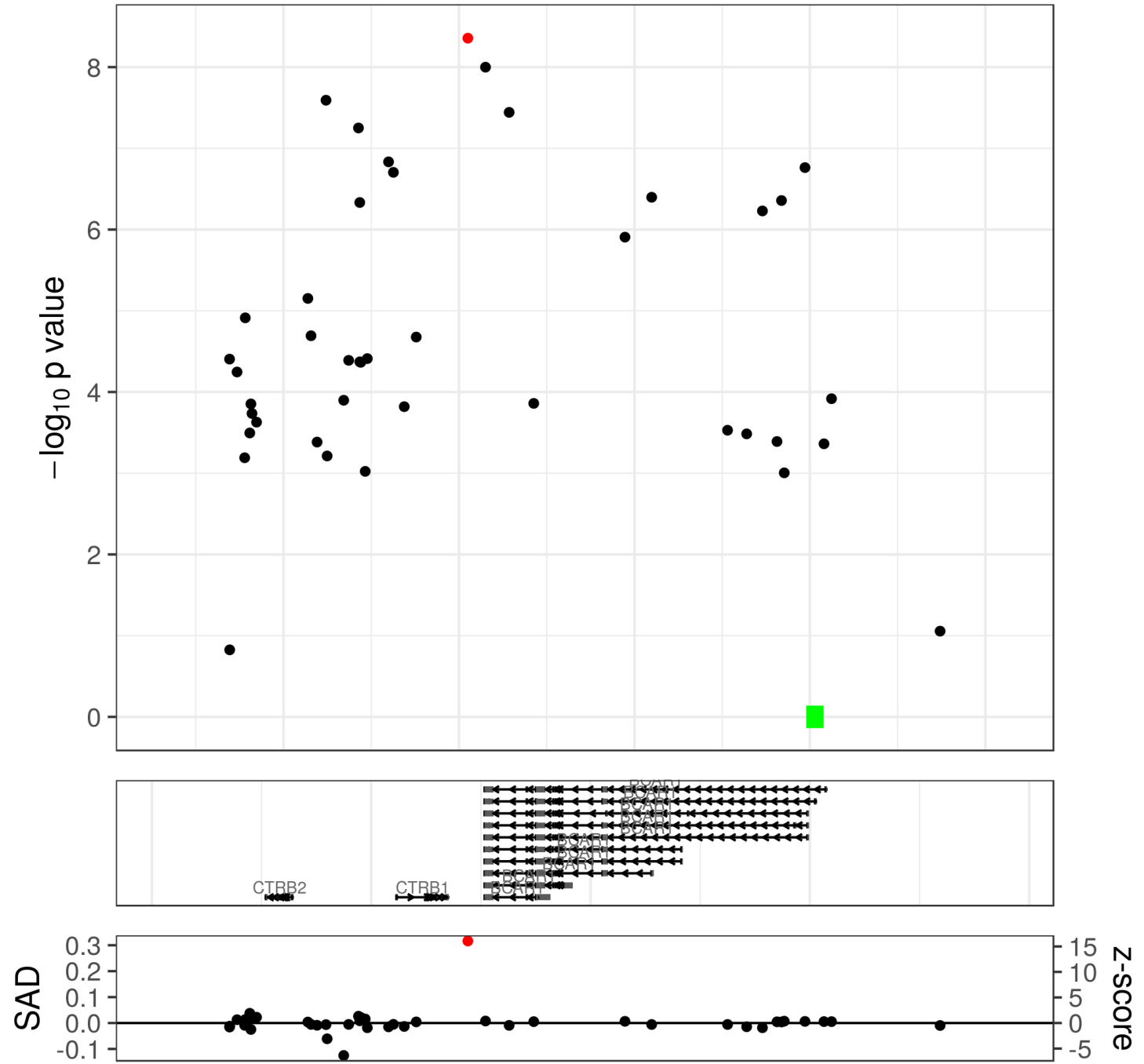
Functional scores from ATAC-seq



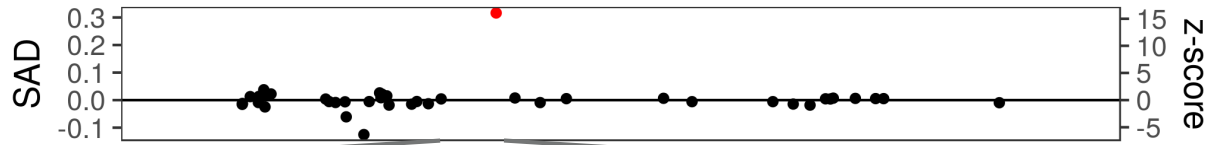
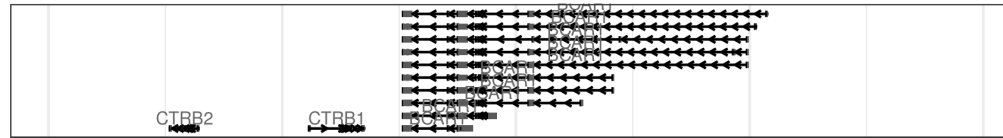
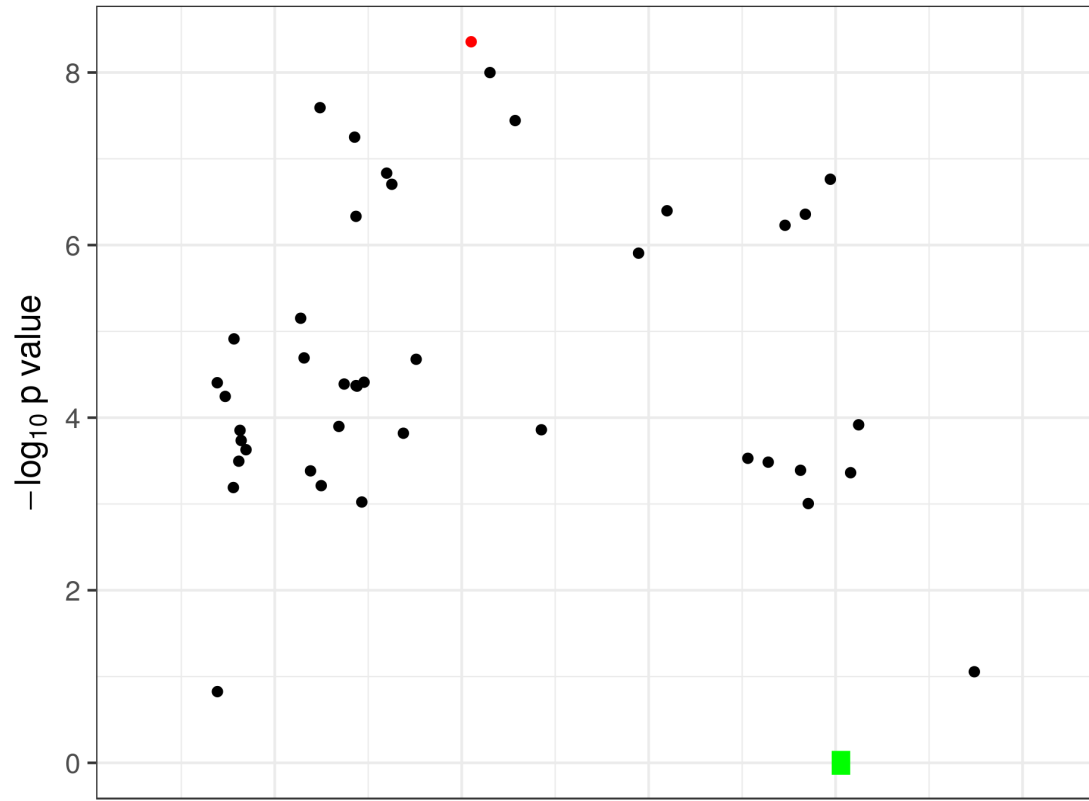
peak166976: 7:117,458,272-117,458,826



peak65926: 16:75,299,578-75,301,561



peak65926: 16:75,299,578-75,301,561



CTGAAAAGGGATGCCCTGAGATCACCATGAGATTGAGGGGCAAGCAGGGCTCACCCCTGACTGGCTCACTTCCCAGGCACGCCCATGAGCCAGGCACGGCCTGCCACCCCTCACTCTCCAGGAAGACCCACCGCGTGGTGGCCGGGATCGTGTGGTGGCCAGGGCGTCTGACCTTGGCTCTCACCCGGAGGCCATCCAGG

