**Supplementary Materials**

**Table S1. Summary of feature annotation.**

|  |  |  |
| --- | --- | --- |
| Class | Description | # Features |
| Mutation pattern | 5bp sequence context centered on each variant site | 5 |
| Changes of TF bindings | Potential change scores of 515 TF bindings mediated by variant | 515 |
| Conservation | Evolutionary conservation of the specific variant nucleotide as measured by PhastCons, GERP and phyloP | 3 |
| Evolutionary conservation of the candidate enhancer region as measured by mean PhastCons, GERP and phyloP score | 3 |
| Negative selection | SNP density calculated from 1000 Genomes Project phase 3 data | 1 |
| Frequency of overlap between the candidate enhancer with sensitive and ultra-sensitive region | 2 |
| Potential TF binding | Frequency of overlap between the candidate enhancer with UCSC transcription factors binding sites | 1 |
| Frequency of overlap between the candidate enhancer with ENCODE motif instances | 1 |
| Epigenetic Activity | Coefficient of variation of 5 histone modifications level (H3K4me1, H3K4me3, H3K27ac, H3K27me3, H3K36me3) across 98 tissue-/cell-types from NIH Roadmap | 5 |
| Maximum signal level of 5 Histone modifications (RPKM) (H3K4me1, H3K4me3, H3K27ac, H3K27me3, H3K36me3) across 98 tissue-/cell-types from NIH Roadmap | 5 |
| Disease feature | Frequency of overlap between the candidate enhancer with GWAS disease SNP | 1 |
| Recurrent features | Frequency of overlap between the candidate enhancer with 6 classes of recurrent regulatory regions (Transcription factor binding peak; DNase I hypersensitive sites; Segway/ChromHMM predicted enhancers; Enhancer distal regulatory modules; site; COSMIC recurrent regulatory variants) | 6 |

**Table S2. Results of five-fold cross validation for down-sampled models.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Training Set | AUC-ROC | Sensitivity | Specificity | Precision | MCC |
| Positive | Negative |
| Set1 | 417 | 407 | 0.909 | 0.8 | 0.92 | 0.91 | 0.72 |
| Set2 | 417 | 407 | 0.908 | 0.79 | 0.9 | 0.9 | 0.7 |
| Set3 | 417 | 407 | 0.901 | 0.79 | 0.9 | 0.89 | 0.69 |
| Set4 | 417 | 407 | 0.907 | 0.8 | 0.89 | 0.89 | 0.7 |
| Set5 | 417 | 407 | 0.901 | 0.79 | 0.88 | 0.88 | 0.68 |
| Set6 | 417 | 407 | 0.91 | 0.79 | 0.93 | 0.92 | 0.72 |
| Set7 | 417 | 407 | 0.909 | 0.78 | 0.92 | 0.91 | 0.71 |
| Set8 | 417 | 407 | 0.913 | 0.8 | 0.91 | 0.9 | 0.71 |
|  |  | Average | 0.907 | 0.79 | 0.906 | 0.9 | 0.7 |