Validation	Baseline model	Trait	Prediction	Difference in prediction accuracy (p-value)				
scheme			accuracy	Gene	Rec.	MNase HS	MAF	GERP
			(p-value)					
Ames-H	DGBLUP	DTS	0.319 (2.9×10 <sup>-11</sup> )	+0.013 (3.3×10 <sup>-4</sup> )	+0.019 (0.021)	+0.007 (0.24)	-0.012 (0.21)	+0.012 (0.015)
$\Rightarrow$ NAM-H		PH	0.259 (8×10 <sup>-10</sup> )	+0.029 (0.023)	+0.007 (0.71)	+0.019 (0.17)	+0.001(0.87)	+0.019 (0.093)
		GY	-0.011 (0.711)	+0.010 (0.085)	+0.025 (3.1×10 <sup>-3</sup> )	+0.012 (0.14)	-0.007 (0.71)	+0.010 (0.16)
	DGBLUP+Gene	DTS	0.332 (1.2×10 <sup>-11</sup> )	-	+0.011 (0.14)	+0.001 (0.74)	N/A	-0.001 (0.55)
		PH	0.288 (1.1×10 <sup>-10</sup> )	-	N/A	-0.002 (0.59)	+0.000(0.97)	-0.006 (0.14)
		GY	-0.001 (0.98)	-	+0.014 (0.015)	+0.003 (0.52)	-0.000 (0.98)	-0.000 (0.99)
NAM-H	GBLUP	DTS	0.497 (4.8×10 <sup>-9</sup> )	-0.000 (0.81)	+0.011 (1.0×10 <sup>-3</sup> )	+0.018 (3.6×10 <sup>-4</sup> )	-0.012 (0.038)	+0.019 (8.6×10 <sup>-5</sup> )
⇒ Ames-H		PH	0.052 (0.079)	+0.078 (1.1×10 <sup>-4</sup> )	+0.052 (1.1×10 <sup>-3</sup> )	+0.072 (7.0×10 <sup>-5</sup> )	+0.006 (1.8×10 <sup>-4</sup> )	+0.071 (6.0×10 <sup>-4</sup> )
		GY	0.254 (2.7×10 <sup>-6</sup> )	-0.014 (0.11)	+0.021 (0.087)	-0.040 (7.1×10 <sup>-3</sup> )	+0.003(0.55)	+0.026 (8.2×10 <sup>-3</sup> )
	GBLUP+Gene	DTS	0.497 (3.8×10 <sup>-9</sup> )	-	+0.013 (2.8×10 <sup>-4</sup> )	+0.019 (4.5×10 <sup>-4</sup> )	-0.022 (4.8×10 <sup>-3</sup> )	+0.019 (1.6×10 <sup>-4</sup> )
		PH	0.131 (2.8×10 <sup>-4</sup> )	-	-0.000 (1.4×10 <sup>-3</sup> )	+0.001 (0.028)	+0.000 (1.6×10 <sup>-3</sup> )	-0.003 (0.42)
		GY	0.240 (1.1×10 <sup>-6</sup> )	-	+0.020 (8.9×10 <sup>-4</sup> )	-0.026 (2.9×10 <sup>-3</sup> )	+0.004 (0.56)	+0.040 (5.4×10 <sup>-6</sup> )

## Table S9 – Prediction accuracy of functional enrichment models

Validation scheme: training panel  $\Rightarrow$  validation panel; Baseline model: DGBLUP (polygenic additive and dominance effects) or DGBLUP+Gene (extension of DGBLUP by gene-proximity annotations) in Ames-H, GBLUP (polygenic additive effects only) or GBLUP+Gene (extension of GBLUP by gene-proximity annotations) in NAM-H; Prediction accuracy: average correlation between observed and predicted phenotypes in validation sets, from the baseline model; Difference in prediction accuracy: difference in prediction accuracy between the baseline model and its extension by one of the following annotations: Gene, proximity to genes ( $\leq 1$  kb of an annotated gene); Rec., recombination rate; MNase HS, chromatin openness; MAF, minor allele frequency; GERP, genomic evolutionary rate profiling score. Significance of average prediction accuracies (non-zero mean) and estimated differences in prediction accuracy (non-zero difference, paired by validation set) was assessed by t-tests. N/A: the fitting algorithm could not converge to a solution.