Supplementary Information for "Partitioning heritability by functional category using genome-wide association summary statistics"

Supplementary note.

Derivation of Equation (1)**.** We begin with a derivation of Equation (1) in a sample with no population structure or other confounding. The derivation of the intercept term in the presence of confounding is identical to the derivation in previous work.[15] We do not assume here that the categories are disjoint.

Let y_i be a quantitative phenotype in individual i, standardized to mean 0 and variance 1 in the population, and let X_{ij} be the genotype of individual i at the j-th SNP, standardized so that for each SNP j, X_{ij} has mean 0 and variance 1 in the population. We will assume a linear model:

$$y_i = \sum_{j \in G} X_{ij} \beta_j(G) + \epsilon_i,$$

where G is some fixed set of SNPs, $\beta_j(G)$ is the effect size of SNP j, and ϵ_i is mean-0 noise.

Letting $M = |G|$, we define $\beta(G) = (\beta_1(G), \ldots, \beta_M(G))$ as the hypothetical result of multiple linear regression of y on X at infinite sample size. Thus, $\beta(G)$ depends on the set G; for example, if G is the set of genotyped SNPs then $\beta_j(G)$ includes the causal effects of non-typed SNPs that are tagged by SNP j, whereas if G contains all SNPs, then $\beta_j(G)$ will reflect only the true effect at SNP j.

We will define the heritability of the set G of SNPs to be

$$h^2_G = \sum_{j \in G} \beta_j(G)^2$$

and the heritability of a category $\mathcal{C} \subset G$ to be

$$h^2_G(\mathcal{C}) = \sum_{j \in \mathcal{C}} \beta_j(G)^2.$$

The definition of $h^2_G(\mathcal{C})$ depends on both G and $\mathcal{C}$; for example, if $\mathcal{C}$ is the set of SNPs with minor allele frequency (MAF) greater than 5%, $h^2_G(\mathcal{C})$ will be larger if $G = \mathcal{C}$ than if G contains SNPs with lower

MAF since in the first case $h^2_G(\mathcal{C})$ includes tagged effects of low-frequency SNPs, whereas in the second case the low-frequency effects are included in $h^2_G(G \setminus \mathcal{C})$. From now on, we will omit the dependence on G, considering it to be fixed.

Suppose that we have a sample of N individuals. Let $y = (y_1, \dots, y_N)$, and let X be the $N \times M$ matrix of standardized genotypes. (We will assume that our sample is large enough that standardizing each SNP within our sample is roughly equivalent to standardizing each SNP in the population.) Let $\epsilon = (\epsilon_1, \dots, \epsilon_N)$ be a vector of residuals. Then we can write

$$y = X\beta + \epsilon.$$

Let $\hat{\beta}_j$ be the estimate of the marginal effect of SNP j in our sample, given by

$$\hat{\beta}_j := \frac{1}{N} X_j^T y,$$

where X_j is the j-th column of X. Define χ^2 statistics $\chi^2_j := N\hat{\beta}^2_j$.

Substituting $y = X\beta + \epsilon$ into the the definition of $\hat{\beta}_j$, we get

$$\begin{aligned}
\hat{\beta}_j &= \frac{1}{N} X_j^T \left(X\beta + \epsilon \right) \\
&= \frac{1}{N} X_j^T X\beta + \frac{1}{N} X_j^T \epsilon \\
&= \sum_k \left(\frac{1}{N} X_j^T X_k \right) \beta_k + \frac{1}{N} X_j^T \epsilon \\
&= \sum_k \hat{r}_{jk} \beta_k + \epsilon'_j
\end{aligned}$$

where $\hat{r}_{jk} := \frac{1}{N} X_j^T X_k$ is the in-sample correlation between SNPs j and k, and $\epsilon'_j = X_j^T \epsilon / N$. Note that ϵ'_j has mean 0 and variance σ_e^2 / N.

We will model β as a mean-0 random vector with independent entries. We allow the variance of β_j to depend on the functional categories that we include in our model; i.e., we have C functional categories $\mathcal{C}_1, \dots, \mathcal{C}_C \subset \{1, \dots, M\}$ and we model the variance of β_j as

$$\mathrm{Var}(\beta_j) = \sum_{c : j \in \mathcal{C}_c} \tau_c. \tag{2}$$

In the case that the $\mathcal{C}_c$ are disjoint, we will have $\tau_c = h^2(\mathcal{C}_c)/M(\mathcal{C}_c)$, where $M(\mathcal{C}_c)$ is the number of

SNPs in $\mathcal{C}_c$. Each SNP must be in at least one category; in practice we either have a set of categories that forms a disjoint partition of the genome, or we include the set of all SNPs as one of the categories.

Consider the expectation of $\chi_j^2 = N\hat{\beta}_j^2$.

$$\begin{aligned}
\mathrm{E}[\chi_j^2] &= N\mathrm{E}\left(\sum_k \hat{r}_{jk}\beta_k + \epsilon'_j\right)^2 \\
&= N\sum_k \hat{r}_{jk}^2 \mathrm{E}[\beta_k^2] + N\mathrm{E}[{\epsilon'}_j^2] \\
&= N\sum_k \hat{r}_{jk}^2 \left(\sum_{c:k\in\mathcal{C}_c} \tau_c\right) + N(\sigma_e^2/N) \\
&= N\sum_c \tau_c \sum_{k\in\mathcal{C}_c} \hat{r}_{jk}^2 + \sigma_e^2,
\end{aligned}$$

where the second equality follows because the random variables are all independent with mean 0.

Let r_{jk} denote the true correlation between SNPs j and k in the underlying population. In an unstructured sample, $\mathrm{E}[\hat{r}_{jk}^2] \approx r_{jk}^2 + 1/N$.

We now have

$$\begin{aligned}
\mathrm{E}[\chi_j^2] &= N\sum_c \tau_c \sum_{c:k\in\mathcal{C}_c} \hat{r}_{jk}^2 + \sigma_e^2 \\
&= N\sum_c \tau_c \sum_{c:k\in\mathcal{C}_c} (\hat{r}_{jk}^2 - 1/N + 1/N) + \sigma_e^2 \\
&= N\sum_c \tau_c \sum_{c:k\in\mathcal{C}_c} (\hat{r}_{jk}^2 - 1/N) + N\sum_c \tau_c \sum_{k\in\mathcal{C}_c} (1/N) + \sigma_e^2 \\
&\approx N\sum_c \tau_c \sum_{k\in\mathcal{C}_c} r_{jk}^2 + \sum_c \sum_{k\in\mathcal{C}_c} \tau_c + \sigma_e^2 \\
&= N\sum_c \tau_c \sum_{k\in\mathcal{C}_c} r_{jk}^2 + \sum_k \sum_{c:k\in\mathcal{C}_c} \tau_c + \sigma_e^2 \\
&= N\sum_c \tau_c \ell(j,c) + \sum_k \mathrm{Var}(\beta_k) + \sigma_e^2,
\end{aligned}$$

where $\ell(j,c) := \sum_{k\in\mathcal{C}_c} r_{jk}^2$. The variance of y_j is $\sum_j \mathrm{Var}(\beta_j) + \sigma_e^2$. Since our phenotype has variance one, we can replace $\sum_j \mathrm{Var}(\beta_j) + \sigma_e^2$ with 1, giving us our main equation:

$$\mathrm{E}[\chi_j^2] = N\sum_c \tau_c \ell(j,c) + 1 \tag{3}$$

An extension of this derivation to case-control traits is in Bulik-Sullivan et al.[47]

Outlier removal. To minimize standard error, we remove outlier SNPs by excluding SNPs j with $\chi_j^2 > \max\{80, 0.001N\}$, where N is the maximum sample size in the study. We also remove the MHC region from all analyses, because of its unusual LD patterns and genetic architecture.

Out-of-bounds estimates. Like other heritability estimation methods, stratified LD score regression can produce heritability estimates that are not between 0 and 1. When unbiasedness is important—for example, when we are averaging estimates over several simulation replicates—we do not adjust these out-of-bounds estimates. However when mean squared error is more important than unbiasedness—for example, when reporting the results of a single analysis—we truncate these estimates to be between 0 and 1. To get a confidence interval around the truncated estimate, we intersect the original confidence interval with the interval $[0, 1]$.

Choice of regression SNPs and reference SNPs. The derivation above does not incorporate imperfect imputation. Ideally, we would prune our χ^2 statistics to a set of "regression SNPs" with imputation accuracy above 0.9, but since imputation accuracy is not always available, we instead use HapMap Project Phase 3 (HapMap3[48]) SNPs as a proxy for well-imputed SNPs. Thus, for the purposes of this paper, regression SNPs are always the HapMap3 SNPs.

However, the choice of which SNPs to include in our regression is distinct from the choice of which SNPs we model as causal. It is important that our model allow as many SNPs as possible to contribute causally, since if we use a model with, for example, only HapMap3 SNPs causal then we are assigning causality of any SNP that is tagged by HapMap3 (but not included in HapMap3) to the HapMap3 SNPs that tag it. This is problematic for functional partitioning because the functional categories containing the causal SNP may not be the same as the functional categories of the HapMap3 SNPs that tag it.

Recall that $h_A^2(B)$ is the heritability of set B defined using a model that allows any SNP in set A to be causal. Another way to restate our above point is that we are interested in $h_{1000G}^2(\mathcal{C})$ rather than $h_{HapMap3}^2(\mathcal{C})$ because a model that only allows HapMap3 SNPs to be causal is allowing non-HapMap3 heritability to be tagged by HapMap3 SNPs and therefore potentially assigning heritability to the wrong functional category. For this reason, our set of potentially causal SNPs—i.e., the set of SNPs in our reference panel—is the set of 9,254,535 1000G SNPs[24] (see Web Resources) with minor allele count greater than five in the 379 European samples.

However, there is a problem introduced by having many reference panel SNPs that are not well-tagged by regression SNPs: it may be inappropriate to extrapolate the enrichments at well-tagged SNPs to the rare SNPs on our reference panel that are not well-tagged. To better understand this issue, recall that stratified LD score regression for disjoint categories works in two steps. First, χ^2 is regressed on $N\ell(j,c)$, and the resulting regression coefficients are (if the categories are disjoint) per-SNP heritabilities in each category. Second, the per-SNP heritability of each category is multiplied by the number of SNPs in that category to obtain an estimate of the heritability in the category. This multiplication involves an implicit assumption that the per-SNP heritability estimate extends uniformly across the whole category. If the per-SNP heritabilities are estimated using HapMap3 SNPs, and the category contains many rare SNPs, this assumption may no longer hold.

SNPs with $MAF > 0.05$ (we denote this set of SNPs $\mathcal{G}$) are generally well-tagged by HapMap3 SNPs. So for any category $\mathcal{C}$, we can estimate $h^2_{1000G}(\mathcal{C}\cap\mathcal{G})$ without potentially inaccurate extrapolation simply by multiplying by the per-SNP heritability by the number of SNPs in $\mathcal{C}\cap\mathcal{G}$ instead of the number of SNPs in $\mathcal{C}$. We do this by default, and the proportions of heritability that we report throughout this manuscript are $h^2_{1000G}(\mathcal{C}\cap\mathcal{G})/h^2_{1000G}(\mathcal{G})$.

Regression weights. There are two considerations for how to weight the regression. First, because of LD, the χ^2 statistics used in the regression are not independent. To correct for this non-independence, we down-weight each SNP in proportion to its LD to the other SNPs used in the regression. The second problem is heteroskedasticity: the χ^2 statistic of a SNP with a high LD score has higher variance than the χ^2 statistic of a SNP with a low LD score, and so we down-weight SNPs with high LD scores.

For over-counting, we compute LD scores within HapMap3 SNPs; call these $\ell_{hm3}(j)$. For heteroskedasticity, we compute $\ell_{1000G}(j,c)$ for all categories c in our model. The variance of χ^2_j is proportional to $(1+N\sum_c \tau_c \ell_{1000G}(j,c))^2$, but we do not have τ_c. We use a rough approximation of τ_c obtained by taking the mean over regression SNPs of both sides of Equation (3) and assuming that all the τ_c are equal. This gives us $\hat{\tau} = \left(\bar{\chi}^2 - 1\right) / \left(N \cdot \bar{\ell}(j)\right)$, where $\bar{\chi}^2$ is the mean of χ^2_j and $\bar{\ell}(j)$ is the mean of $\sum_c \ell_{1000G}(j,c)$, both taken over regression SNPs. We then weight SNP j by the inverse product of the over counting weights and heteroskedasticity weights:

$$w_j \coloneqq \frac{1}{\ell_{hm3}(j)(1+N\hat{\tau}\sum_c \ell_{1000G}(j,c))^2}.$$

Analyzing summary statistics with GC correction. Artificial deflation of χ^2 statistics by GC correction causes an equal deflation in the estimates of category-specific heritability and total heritability. Because these two estimates are deflated by the same amount, though,[15] the estimate of proportion of heritability is unaffected. Moreover, statistical tests for heritability enrichment and for $\tau_c > 0$ remain valid.

Many of the datasets analyzed in this paper have GC correction applied, and so we report proportions of heritability, enrichment, and z-scores/p-values, but we do not report estimates of total heritability or of category-specific heritability.

Partitioned heritability vs. regression coefficients. The parameters τ_c and $h^2(\mathcal{C})$ have different interpretations. Because $h^2(\mathcal{C})$ is defined as the sum of squared effects of SNPs in $\mathcal{C}$, it should not depend on the categories chosen to be in the model, and is generally a robust quantity to estimate. On the other hand, τ_c is the contribution of category $\mathcal{C}_c$ after controlling for all other categories in the model; it is defined by the equation $\mathrm{Var}(\beta_j) = \sum_{c:j\in\mathcal{C}_c} \tau_c$ and depends explicitly on the choice of categories to put in the model.

As a result, $h^2(\mathcal{C}_c)$ is a more robust quantity, and we report this value as the outcome of our baseline analysis. On the other hand, when comparing cell types, we believe that it is important to control for the overlap of cell-type-specific annotations with other functional categories such as coding. Thus, we rank cell types by the P-value of τ_c, rather than the P-value of total enrichment, (Prop. h^2) / (Prop. SNPs).

Simulations: Supplementary Figures 2 and 3. The data for these two figures is the same as for Figure 1, but here we plot point estimates to assess bias, rather than plotting rejection probabilities to assess power. In Supplementary Figure 2, we display results from the data simulated to have enrichment in the CNS cell-type group, and in Supplementary Figure 3 display results from the null simulations.

Heritability z-score method for deciding which phenotypes are amenable to stratified LD score regression. We wanted to run our method on phenotypes for which we would get meaningful results, but we did not want to filter results by what the standard errors were around our estimates. A phenotype will give low standard errors if it is sufficiently polygenic and has high enough sample size and heritability. It is hard to know ahead of time how polygenic a trait is, but these three dimensions are conveniently captured in the z-score of total SNP-heritability, which increases with $N \cdot h_g^2$ and with proportion of causal SNPs (Figure 1b, and which corresponds closely to power to detect enrichment (Figure 1c). We chose a cutoff of z-score > 7 for this paper. The z-scores of the datasets analyzed in this paper appear in Supplementary Table 8.

Nh_g^2 method for deciding which phenotypes are amenable to stratified LD score regression. An alternative method for choosing which phenotypes are amenable to our method is to use a cutoff of Nh_g^2. The disadvantage is that this statistic does not take into account polygenicity, which is an important determinant of power (Figure 1a). We did not use this as a criterion in this work, but we recommend it to potential users of our method who would like to get a rough idea of whether their dataset has sufficient sample size. In our simulations, a heritability z-score of 7 corresponds to Nh_g^2 of roughly 4,500 for very polygenic traits, and Nh_g^2 of roughly 12,500 for less polygenic traits (Figure 1b).

Choice of 17 phenotypes to include in the main analysis. We quantified the combination of sample size and heritability by the z-score of total SNP-heritability in the baseline analysis (see "Heritability z-score method for deciding which phenotypes are amenable to stratified LD score regression" above). We applied our method to all traits with available summary statistics, and removed all traits with a heritability z-score less than 7. We then removed one of each pair of traits with a large genetic correlation (> 0.95): we removed college attendance, which has a very high genetic correlation with years of education, and total cholesterol, which has a very high genetic correlation with LDL.[47]

For Crohn's disease and ulcerative colitis, we used a dataset with 1000 Genomes imputation which was newer than the dataset available at the link in Online Methods.

Choice of nine traits to include in the meta-analysis of traits For our meta-analysis over traits, we identified pairs of traits with substantial sample overlap and trait correlation by using the intercept of cross-trait LD score regression.[47] Specifically, for each pair of traits, we computed the genetic covariance intercept on the N1N2 scale, which for quantitative traits estimates phenotypic correlation times sample overlap, and for case-control estimates a related quantity that is high, for example, if two unrelated traits share controls ([47]). This intercept is downwardly biased in the presence of GC correction, so we divided by the square root of the product of the heritability estimates of the two traits to correct for this bias. We identified pairs of traits for which this quantity was at least 15% of the sample size of either of the traits, and we excluded one of each such pair. The remaining set of traits was: Height, BMI, menarche, LDL levels, coronary artery disease, schizophrenia, educational attainment, smoking behavior, and rheumatoid arthritis.

Choice of traits to include in Figure 5 (Enrichment estimates for selected annotations and traits). Height, BMI, age at menarche, and schizophrenia are the four traits with the highest combination of SNP-heritability and sample size, which we quantify by the z-score of total heritability in the full baseline analysis. We also included a meta-analysis of immunological diseases, since they have a different pattern of enrichment from other traits; for example FANTOM5 enhancers are very enriched for immunological diseases but not for other traits. This meta-analysis included rheumatoid arthritis and an inflammatory bowel disease dataset that included both Crohn's disease and ulcerative colitis as cases; we did not include Crohn's disease and ulcerative colitis separately since the two studies share controls.

Cell-type specific analysis. We used all available cell types from the four histone marks, excluding cell lines and cells labeled as cultured cells to limit ourselves to data with the clearest biological interpretation. The resulting cell-type-specific annotations are listed in Supplementary Table 2.

Custom genotyping arrays. Stratified LD score regression is not currently applicable to studies using a custom genotyping arrays. For these arrays, SNPs that are more likely to be in large-effect loci also have better coverage, and this dependency is not modeled in the above derivation. In a meta-analysis of several studies, some of which have custom genotyping arrays, coverage is still dependent on effect size in a way that violates model assumptions.

Cell-type-specificity of super-enhancers. We were interested in whether we would get increased signal from a cell-type-specific analysis using super-enhancers compared to regular enhancers, and compared to the four histone marks we used in our primary analysis. To test this, we repeated the cell-type-specific analysis described above for super-enhancers and regular enhancers from Hnisz et al.,[18] obtaining a z-score for each cell type in each of six marks (four marks from the primary analysis, plus regular enhancers and super-enhancers from Hnisz et al). Then, for each of the six marks, we computed the average over traits of the highest z-score achieved by any cell type for that trait, obtaining a score that should be higher for a mark with a stronger cell-type-specific signal.

Super-enhancers did not receive a higher score than regular enhancers. In fact, the average top z-score for super-enhancers was 3.0, while the average top z-score for regular enhancers was 4.7. The average top z-scores for the four histone marks used in the primary analysis were 4.9, 3.7, 3.5, and 4.5, respectively.

Power as a function of annotation size. Stratified LD score regression has more power to detect enrichment in large categories than in small categories. To quantify this, we performed simulations in which the CNS cell-type group annotation was pruned to be 0.25x, 0.5x, 0.75x, or 1.0x the original size by choosing to drop or keep each region with equal probability. We then simulated phenotypes and summary statistics with the same baseline enrichment, and with enrichment in this new annotation that matched the enrichment of the original CNS cell-type group annotation. We then plotted probability of rejection; the results are displayed in Figure 8 and show a strong dependence of power on category size.

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Annotation	Prop. SNPs	Mean segment length (bp)
Coding	0.015	315
Conserved	0.026	34
CTCF	0.024	490
DGF	0.138	208
DHS	0.168	358
FANTOM5 Enhancer	0.004	289
Enhancer	0.063	678
Fetal DHS	0.085	339
H3K27ac[18]	0.391	12411
H3K27ac[17]	0.269	1051
H3K4me1	0.427	1676
H3K4me3	0.133	941
H3K9ac	0.126	964
Intron	0.387	6537
PromoterFlanking	0.008	266
Promoter	0.031	4192
Repressed	0.461	572
Super-enhancer	0.168	54744
TFBS	0.132	509
Transcribed	0.345	484
TSS	0.018	813
3-prime UTR	0.011	844
5-prime UTR	0.005	197
Weak Enhancer	0.021	249

Supplementary Table 1: Annotations used. For DHS, H3K4me1, H3K4me3, and H3K9ac, we include peaks and regions as two annotations. For the annotations from the Hoffman segmentation,[19] we union over six cell lines for each category except Repressed, where we take an intersection instead. We also include a 500bp window around each annotation as a separate annotation in the model.

Cell type	Mark	Cell-type group
Fetal adrenal	H3K4me1	Adrenal/Pancreas
Fetal adrenal	H3K4me3	Adrenal/Pancreas
Pancreas	H3K4me1	Adrenal/Pancreas
Pancreas	H3K4me3	Adrenal/Pancreas
Pancreatic islets	H3K27ac	Adrenal/Pancreas
Pancreatic islets	H3K4me1	Adrenal/Pancreas
Pancreatic islets	H3K4me1	Adrenal/Pancreas
Pancreatic islets	H3K4me3	Adrenal/Pancreas
Pancreatic islets	H3K4me3	Adrenal/Pancreas
Pancreatic islets	H3K9ac	Adrenal/Pancreas
Angular gyrus	H3K27ac	CNS
Angular gyrus	H3K4me1	CNS
Angular gyrus	H3K4me3	CNS
Angular gyrus	H3K9ac	CNS
Anterior caudate	H3K27ac	CNS
Anterior caudate	H3K4me1	CNS
Anterior caudate	H3K4me3	CNS
Anterior caudate	H3K9ac	CNS
Cingulate gyrus	H3K27ac	CNS
Cingulate gyrus	H3K4me1	CNS
Cingulate gyrus	H3K4me3	CNS
Cingulate gyrus	H3K9ac	CNS
Fetal brain	H3K4me1	CNS
Fetal brain	H3K4me3	CNS
Fetal brain	H3K4me3	CNS
Fetal brain	H3K9ac	CNS
Germinal matrix	H3K4me3	CNS
Hippocampus middle	H3K27ac	CNS
Hippocampus middle	H3K4me1	CNS
Hippocampus middle	H3K4me3	CNS
Hippocampus middle	H3K9ac	CNS
Inferior temporal lobe	H3K27ac	CNS
Inferior temporal lobe	H3K4me1	CNS
Inferior temporal lobe	H3K4me3	CNS
Inferior temporal lobe	H3K9ac	CNS
Mid frontal lobe	H3K27ac	CNS
Mid frontal lobe	H3K4me1	CNS
Mid frontal lobe	H3K4me3	CNS
Mid frontal lobe	H3K9ac	CNS

Neurosphere	H3K27ac	CNS
Substantia nigra	H3K27ac	CNS
Substantia nigra	H3K4me1	CNS
Substantia nigra	H3K4me3	CNS
Substantia nigra	H3K9ac	CNS
Aorta	H3K4me3	Cardiovascular
Fetal heart	H3K4me1	Cardiovascular
Fetal heart	H3K4me3	Cardiovascular
Fetal heart	H3K9ac	Cardiovascular
Fetal lung	H3K4me1	Cardiovascular
Fetal lung	H3K4me3	Cardiovascular
Fetal lung	H3K9ac	Cardiovascular
Left Ventricle	H3K4me1	Cardiovascular
Left Ventricle	H3K4me3	Cardiovascular
Lung	H3K4me1	Cardiovascular
Lung	H3K4me3	Cardiovascular
Right atrium	H3K4me1	Cardiovascular
Right atrium	H3K4me3	Cardiovascular
Right ventricle	H3K4me1	Cardiovascular
Right ventricle	H3K4me3	Cardiovascular
Breast fibroblast primary	H3K4me1	Connective/Bone
Breast fibroblast primary	H3K4me3	Connective/Bone
Chondrogenic dif	H3K27ac	Connective/Bone
Osteoblast	H3K27ac	Connective/Bone
Penis foreskin fibroblast primary	H3K4me1	Connective/Bone
Penis foreskin fibroblast primary	H3K4me3	Connective/Bone
Colon smooth muscle	H3K27ac	Gastrointestinal
Colon smooth muscle	H3K4me1	Gastrointestinal
Colon smooth muscle	H3K4me3	Gastrointestinal
Colon smooth muscle	H3K9ac	Gastrointestinal
Colonic mucosa	H3K27ac	Gastrointestinal
Colonic mucosa	H3K4me1	Gastrointestinal
Colonic mucosa	H3K4me3	Gastrointestinal
Colonic mucosa	H3K9ac	Gastrointestinal
Duodenum Mucosa	H3K4me1	Gastrointestinal
Duodenum Mucosa	H3K4me3	Gastrointestinal
Duodenum Mucosa	H3K9ac	Gastrointestinal
Duodenum mucosa	H3K27ac	Gastrointestinal
Duodenum smooth muscle	H3K27ac	Gastrointestinal
Duodenum smooth muscle	H3K4me1	Gastrointestinal

Duodenum smooth muscle	H3K4me3	Gastrointestinal
Esophagus	H3K4me1	Gastrointestinal
Esophagus	H3K4me3	Gastrointestinal
Fetal large intestine	H3K4me1	Gastrointestinal
Fetal large intestine	H3K4me3	Gastrointestinal
Fetal small intestine	H3K4me1	Gastrointestinal
Fetal small intestine	H3K4me3	Gastrointestinal
Fetal stomach	H3K4me1	Gastrointestinal
Fetal stomach	H3K4me3	Gastrointestinal
Gastric	H3K4me1	Gastrointestinal
Gastric	H3K4me3	Gastrointestinal
Rectal mucosa	H3K27ac	Gastrointestinal
Rectal mucosa	H3K4me1	Gastrointestinal
Rectal mucosa	H3K4me3	Gastrointestinal
Rectal mucosa	H3K9ac	Gastrointestinal
Rectal smooth muscle	H3K27ac	Gastrointestinal
Rectal smooth muscle	H3K4me1	Gastrointestinal
Rectal smooth muscle	H3K4me3	Gastrointestinal
Rectal smooth muscle	H3K9ac	Gastrointestinal
Sigmoid colon	H3K4me1	Gastrointestinal
Sigmoid colon	H3K4me3	Gastrointestinal
Small intestine	H3K4me1	Gastrointestinal
Small intestine	H3K4me3	Gastrointestinal
Stomach mucosa	H3K4me1	Gastrointestinal
Stomach mucosa	H3K4me3	Gastrointestinal
Stomach mucosa	H3K9ac	Gastrointestinal
Stomach smooth muscle	H3K27ac	Gastrointestinal
Stomach smooth muscle	H3K4me1	Gastrointestinal
Stomach smooth muscle	H3K4me3	Gastrointestinal
Stomach smooth muscle	H3K9ac	Gastrointestinal
CD14	H3K27ac	Immune
CD14 primary	H3K4me1	Immune
CD14 primary	H3K4me3	Immune
CD15 primary	H3K4me1	Immune
CD15 primary	H3K4me3	Immune
CD19	H3K27ac	Immune
CD19 primary (BI)	H3K4me1	Immune
CD19 primary (BI)	H3K4me3	Immune
CD19 primary (UW)	H3K4me1	Immune
CD19 primary (UW)	H3K4me3	Immune

CD20	H3K27ac	Immune
CD25+ CD127- Treg	H3K27ac	Immune
CD25- CD45RA+ naive	H3K27ac	Immune
CD25- IL17+ Th17 stim	H3K27ac	Immune
CD25- IL17- Th stim MACS	H3K27ac	Immune
CD25int CD127+ Tmem	H3K27ac	Immune
CD3 primary	H3K27ac	Immune
CD3 primary (BI)	H3K4me1	Immune
CD3 primary (BI)	H3K4me3	Immune
CD3 primary (UW)	H3K4me1	Immune
CD3 primary (UW)	H3K4me3	Immune
CD34 primary	H3K4me1	Immune
CD34 primary	H3K4me3	Immune
CD4 memory primary	H3K4me1	Immune
CD4 memory primary	H3K4me3	Immune
CD4 naive primary	H3K4me1	Immune
CD4 naive primary	H3K4me3	Immune
CD4 primary	H3K4me3	Immune
CD4+ CD25+ CD127- Treg primary	H3K4me1	Immune
CD4+ CD25+ CD127- Treg primary	H3K4me3	Immune
CD4+ CD25- CD45R0+ memory primary	H3K4me1	Immune
CD4+ CD25- CD45R0+ memory primary	H3K4me3	Immune
CD4+ CD25- CD45RA+ naive primary	H3K4me1	Immune
CD4+ CD25- CD45RA+ naive primary	H3K4me3	Immune
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary	H3K4me1	Immune
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary	H3K4me3	Immune
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th primary	H3K4me1	Immune
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th primary	H3K4me3	Immune
CD4+ CD25- Th primary	H3K4me1	Immune
CD4+ CD25- Th primary	H3K4me3	Immune
CD4+ CD25int CD127+ Tmem primary	H3K4me1	Immune
CD4+ CD25int CD127+ Tmem primary	H3K4me3	Immune
CD56 primary	H3K4me1	Immune
CD56 primary	H3K4me3	Immune
CD8 memory primary	H3K4me1	Immune
CD8 memory primary	H3K4me3	Immune
CD8 naive primary (BI)	H3K4me1	Immune
CD8 naive primary (BI)	H3K4me3	Immune
CD8 naive primary (UCSF-UBC)	H3K4me1	Immune
CD8 naive primary (UCSF-UBC)	H3K4me3	Immune

CD8 naive primary (UCSF-UBC)	H3K9ac	Immune
CD8 primary	H3K4me3	Immune
Fetal thymus	H3K4me1	Immune
Fetal thymus	H3K4me3	Immune
Mobilized CD34	H3K27ac	Immune
Mobilized CD34 primary	H3K4me1	Immune
Mobilized CD34 primary	H3K4me3	Immune
Peripheralblood mononuclear primary	H3K4me1	Immune
Peripheralblood mononuclear primary	H3K4me3	Immune
Peripheralblood mononuclear primary	H3K9ac	Immune
Spleen	H3K4me1	Immune
Spleen	H3K4me3	Immune
Th0	H3K27ac	Immune
Th1	H3K27ac	Immune
Th2	H3K27ac	Immune
Thymus	H3K4me1	Immune
Treg primary	H3K4me3	Immune
Fetal kidney	H3K9ac	Kidney
Kidney	H3K27ac	Kidney
Kidney	H3K4me1	Kidney
Kidney	H3K4me3	Kidney
Kidney	H3K9ac	Kidney
Liver	H3K27ac	Liver
Liver (BI)	H3K4me1	Liver
Liver (BI)	H3K4me3	Liver
Liver (BI)	H3K9ac	Liver
Liver (UCSD)	H3K4me1	Liver
Liver (UCSD)	H3K4me3	Liver
Adipose nuclei	H3K27ac	Other
Adipose nuclei	H3K4me1	Other
Adipose nuclei	H3K4me3	Other
Adipose nuclei	H3K9ac	Other
Breast luminal epithelial	H3K4me1	Other
Breast myoepithelial	H3K4me1	Other
Breast myoepithelial	H3K4me3	Other
Breast myoepithelial	H3K9ac	Other
Breast vHMEC	H3K4me1	Other
Breast vHMEC	H3K4me3	Other
Fetal placenta	H3K4me1	Other
Fetal placenta	H3K4me3	Other

Ovary	H3K4me1	Other
Ovary	H3K4me3	Other
Penis foreskin keratinocyte primary	H3K4me1	Other
Penis foreskin keratinocyte primary	H3K4me3	Other
Penis foreskin keratinocyte primary	H3K9ac	Other
Penis foreskin melanocyte primary	H3K4me1	Other
Penis foreskin melanocyte primary	H3K4me3	Other
Placenta amnion	H3K4me1	Other
Placenta amnion	H3K4me3	Other
Placenta chorion	H3K4me1	Other
Placenta chorion	H3K4me3	Other
Fetal leg muscle	H3K4me1	Skeletal muscle
Fetal leg muscle	H3K4me3	Skeletal muscle
Fetal trunk muscle	H3K4me1	Skeletal muscle
Fetal trunk muscle	H3K4me3	Skeletal muscle
Psoas muscle	H3K4me1	Skeletal muscle
Psoas muscle	H3K4me3	Skeletal muscle
Skeletal muscle	H3K27ac	Skeletal muscle
Skeletal muscle	H3K4me1	Skeletal muscle
Skeletal muscle	H3K4me3	Skeletal muscle
Skeletal muscle	H3K9ac	Skeletal muscle

Supplementary Table 2: Cell types used in the cell-type-specific analysis. When the same cell type in the same histone mark from more than one institution was used, the institution is given in parentheses.

Phenotype	Reference/consortium	N
Height	Lango Allen et al., 2010 Nature	133,858
BMI	Speliotes et al., 2010 Nat Genet	123,912
Age at menarche	Perry et al., 2014 Nature	132,989
LDL	Teslovich et al., 2010 Nature	95,454
HDL	Teslovich et al., 2010 Nature	99,900
Triglycerides	Teslovich et al., 2010 Nature	96,598
Coronary Artery Disease	Schunkert et al., Nat Genet 2011	86,995
Type-2 Diabetes	Morris et al., 2012 Nat Genet	69,033
Fasting glucose	Manning et. al., Nat Genet, 2012	46,186
Schizophrenia	SCZ Working Group of the PGC, 2014 Nature	70,100
Bipolar Disorder	Bip Working Group of the PGC, 2011 Nat Genet	16,731
Anorexia	Boraska et al., 2014 Mol Psych	17,767
Educational attainment	Rietveld et al., Science 2013	101,069
Ever smoked	TAG Consortium, 2010 Nat Genet	74,035
Rheumatoid Arthritis	Okada et al., 2014 Nature	38,242
Crohn's Disease	Jostins et al., 2012 Nature	20,883
Ulcerative Colitis	Jostins et al., 2012 Nature	27,432

Supplementary Table 3: Phenotypes used in the main analyses. The average sample size is 73,599.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.104 (0.012)	7.124 (0.842)	0.000
Coding + 500bp	0.065	0.190 (0.030)	2.937 (0.467)	0.000
Conserved	0.026	0.347 (0.039)	13.318 (1.503)	0.000
Conserved + 500bp	0.333	0.654 (0.026)	1.967 (0.078)	0.000
CTCF	0.024	-0.004 (0.019)	-0.165 (0.792)	0.404
CTCF + 500bp	0.071	0.059 (0.019)	0.824 (0.273)	0.456
DGF	0.138	0.358 (0.094)	2.602 (0.686)	0.020
DGF + 500bp	0.542	0.761 (0.069)	1.406 (0.128)	0.003
DHS peaks	0.112	0.224 (0.063)	2.004 (0.566)	0.056
DHS	0.168	0.285 (0.069)	1.698 (0.410)	0.076
DHS + 500bp	0.499	0.787 (0.041)	1.579 (0.081)	0.000
FANTOM5 Enhancer	0.004	-0.003 (0.009)	-0.727 (2.156)	0.536
FANTOM5 Enhancer + 500bp	0.019	0.017 (0.017)	0.880 (0.896)	0.743
Enhancer	0.063	0.239 (0.050)	3.767 (0.783)	0.000
Enhancer + 500bp	0.154	0.359 (0.042)	2.334 (0.272)	0.000
Fetal DHS	0.085	0.238 (0.044)	2.809 (0.513)	0.001
Fetal DHS + 500bp	0.285	0.590 (0.058)	2.071 (0.204)	0.000
H3K27ac[18]	0.391	0.630 (0.054)	1.612 (0.138)	0.000
H3K27ac[18] + 500bp	0.423	0.664 (0.059)	1.572 (0.140)	0.000
H3K27ac[17]	0.269	0.490 (0.054)	1.818 (0.200)	0.000
H3K27ac[17] + 500bp	0.336	0.611 (0.040)	1.818 (0.118)	0.000
H3K4me1 peaks	0.171	0.447 (0.040)	2.611 (0.236)	0.000
H3K4me1	0.427	0.792 (0.065)	1.857 (0.152)	0.000
H3K4me1 + 500bp	0.609	0.910 (0.039)	1.493 (0.064)	0.000
H3K4me3 peaks	0.042	0.158 (0.025)	3.775 (0.602)	0.000
H3K4me3	0.133	0.344 (0.045)	2.583 (0.336)	0.000
H3K4me3 + 500bp	0.255	0.487 (0.056)	1.905 (0.220)	0.000
H3K9ac peaks	0.039	0.248 (0.024)	6.396 (0.618)	0.000
H3K9ac	0.126	0.408 (0.056)	3.233 (0.441)	0.000
H3K9ac + 500bp	0.231	0.503 (0.040)	2.183 (0.172)	0.000
Intron	0.387	0.462 (0.014)	1.192 (0.035)	0.005
Intron + 500bp	0.397	0.521 (0.015)	1.313 (0.037)	0.000
PromoterFlanking	0.008	0.004 (0.011)	0.448 (1.315)	0.617
PromoterFlanking + 500bp	0.033	0.081 (0.018)	2.433 (0.532)	0.021
Promoter	0.031	0.087 (0.016)	2.807 (0.513)	0.008
Promoter + 500bp	0.039	0.080 (0.016)	2.061 (0.424)	0.018
Repressed	0.461	0.285 (0.063)	0.618 (0.137)	0.006
Repressed + 500bp	0.719	0.446 (0.049)	0.620 (0.068)	0.000
Super Enhancer	0.168	0.304 (0.035)	1.803 (0.209)	0.000
Super Enhancer + 500bp	0.172	0.319 (0.037)	1.856 (0.216)	0.000
TFBS	0.132	0.445 (0.063)	3.356 (0.478)	0.000
TFBS + 500bp	0.343	0.503 (0.052)	1.465 (0.152)	0.005
Transcribed	0.345	0.407 (0.038)	1.178 (0.111)	0.251
Transcribed + 500bp	0.763	0.721 (0.028)	0.945 (0.036)	0.104
TSS	0.018	0.104 (0.023)	5.685 (1.281)	0.001
TSS + 500bp	0.035	0.172 (0.029)	4.948 (0.830)	0.000
3-prime UTR	0.011	0.054 (0.009)	4.891 (0.857)	0.005
3-prime UTR + 500bp	0.027	0.074 (0.011)	2.731 (0.411)	0.003
5-prime UTR	0.005	0.028 (0.008)	5.240 (1.387)	0.008
5-prime UTR + 500bp	0.028	0.065 (0.010)	2.341 (0.375)	0.001
Weak Enhancer	0.021	0.070 (0.023)	3.325 (1.090)	0.001
Weak Enhancer + 500bp	0.089	0.199 (0.030)	2.238 (0.335)	0.000

Supplementary Table 4: Proportion of SNP-heritability and enrichment for different functional categories. We display results meta-analyzed across nine traits for each of the 53 annotations, including two distinct H3K27ac annotations (see Online Methods). Although true SNP-heritability is non-negative, we report here unbiased estimates, we can be negative (see “Out-of-bounds estimates”).

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.127 (0.036)	8.661 (2.481)	0.002
Coding + 500bp	0.065	0.192 (0.034)	2.979 (0.521)	0.000
Conserved	0.026	0.340 (0.051)	13.029 (1.949)	0.000
Conserved + 500bp	0.333	0.636 (0.053)	1.913 (0.158)	0.000
CTCF	0.024	0.050 (0.046)	2.118 (1.910)	0.558
CTCF + 500bp	0.071	0.089 (0.047)	1.249 (0.668)	0.709
DGF	0.138	0.585 (0.085)	4.253 (0.620)	0.000
DGF + 500bp	0.542	0.983 (0.066)	1.815 (0.123)	0.000
DHS peaks	0.112	0.429 (0.107)	3.837 (0.957)	0.004
DHS	0.168	0.512 (0.120)	3.050 (0.716)	0.005
DHS + 500bp	0.499	0.787 (0.062)	1.579 (0.125)	0.000
FANTOM5 Enhancer	0.004	0.013 (0.019)	2.930 (4.429)	0.664
FANTOM5 Enhancer + 500bp	0.019	0.014 (0.023)	0.711 (1.225)	0.813
Enhancer	0.063	0.184 (0.064)	2.906 (1.017)	0.061
Enhancer + 500bp	0.154	0.396 (0.054)	2.573 (0.353)	0.000
Fetal DHS	0.085	0.281 (0.089)	3.311 (1.049)	0.029
Fetal DHS + 500bp	0.285	0.504 (0.080)	1.770 (0.280)	0.006
H3K27ac[18]	0.391	0.782 (0.035)	1.999 (0.089)	0.000
H3K27ac[18] + 500bp	0.423	0.780 (0.043)	1.846 (0.101)	0.000
H3K27ac[17]	0.269	0.533 (0.066)	1.978 (0.243)	0.000
H3K27ac[17] + 500bp	0.336	0.674 (0.061)	2.005 (0.181)	0.000
H3K4me1 peaks	0.171	0.422 (0.091)	2.465 (0.530)	0.006
H3K4me1	0.427	0.965 (0.074)	2.261 (0.173)	0.000
H3K4me1 + 500bp	0.609	0.946 (0.036)	1.553 (0.060)	0.000
H3K4me3 peaks	0.042	0.075 (0.053)	1.791 (1.262)	0.530
H3K4me3	0.133	0.429 (0.071)	3.215 (0.531)	0.000
H3K4me3 + 500bp	0.255	0.584 (0.054)	2.286 (0.212)	0.000
H3K9ac peaks	0.039	0.266 (0.060)	6.851 (1.542)	0.000
H3K9ac	0.126	0.558 (0.065)	4.428 (0.519)	0.000
H3K9ac + 500bp	0.231	0.602 (0.055)	2.612 (0.237)	0.000
Intron	0.387	0.448 (0.031)	1.156 (0.081)	0.055
Intron + 500bp	0.397	0.532 (0.025)	1.340 (0.064)	0.000
PromoterFlanking	0.008	-0.046 (0.025)	-5.400 (3.020)	0.038
PromoterFlanking + 500bp	0.033	0.116 (0.034)	3.453 (1.029)	0.017
Promoter	0.031	0.089 (0.033)	2.848 (1.057)	0.079
Promoter + 500bp	0.039	0.101 (0.020)	2.603 (0.528)	0.003
Repressed	0.461	0.115 (0.093)	0.248 (0.202)	0.000
Repressed + 500bp	0.719	0.369 (0.038)	0.513 (0.054)	0.000
Super Enhancer	0.168	0.384 (0.026)	2.280 (0.154)	0.000
Super Enhancer + 500bp	0.172	0.398 (0.024)	2.317 (0.137)	0.000
TFBS	0.132	0.455 (0.083)	3.438 (0.629)	0.000
TFBS + 500bp	0.343	0.682 (0.065)	1.984 (0.190)	0.000
Transcribed	0.345	0.572 (0.094)	1.657 (0.273)	0.018
Transcribed + 500bp	0.763	0.652 (0.052)	0.854 (0.068)	0.032
TSS	0.018	0.107 (0.038)	5.853 (2.107)	0.020
TSS + 500bp	0.035	0.174 (0.032)	4.991 (0.906)	0.000
3-prime UTR	0.011	0.102 (0.032)	9.240 (2.858)	0.005
3-prime UTR + 500bp	0.027	0.118 (0.032)	4.380 (1.176)	0.004
5-prime UTR	0.005	0.045 (0.022)	8.310 (4.068)	0.073
5-prime UTR + 500bp	0.028	0.069 (0.023)	2.470 (0.841)	0.084
Weak Enhancer	0.021	0.018 (0.043)	0.853 (2.025)	0.942
Weak Enhancer + 500bp	0.089	0.109 (0.048)	1.229 (0.540)	0.670

(a) Height

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.104 (0.027)	7.071 (1.809)	0.001
Coding + 500bp	0.065	0.129 (0.032)	1.992 (0.501)	0.051
Conserved	0.026	0.508 (0.059)	19.504 (2.259)	0.000
Conserved + 500bp	0.333	0.545 (0.068)	1.640 (0.205)	0.001
CTCF	0.024	-0.027 (0.049)	-1.135 (2.046)	0.289
CTCF + 500bp	0.071	0.025 (0.046)	0.358 (0.643)	0.322
DGF	0.138	0.034 (0.123)	0.249 (0.897)	0.405
DGF + 500bp	0.542	0.674 (0.068)	1.244 (0.125)	0.050
DHS peaks	0.112	0.125 (0.100)	1.123 (0.893)	0.891
DHS	0.168	0.093 (0.123)	0.554 (0.731)	0.543
DHS + 500bp	0.499	0.890 (0.122)	1.785 (0.246)	0.003
FANTOM5 Enhancer	0.004	0.003 (0.018)	0.792 (4.138)	0.960
FANTOM5 Enhancer + 500bp	0.019	-0.004 (0.026)	-0.218 (1.364)	0.372
Enhancer	0.063	0.259 (0.053)	4.083 (0.833)	0.000
Enhancer + 500bp	0.154	0.305 (0.052)	1.980 (0.335)	0.003
Fetal DHS	0.085	0.112 (0.088)	1.320 (1.042)	0.757
Fetal DHS + 500bp	0.285	0.572 (0.081)	2.008 (0.283)	0.001
H3K27ac[18]	0.391	0.514 (0.037)	1.315 (0.095)	0.001
H3K27ac[18] + 500bp	0.423	0.564 (0.039)	1.334 (0.093)	0.001
H3K27ac[17]	0.269	0.447 (0.059)	1.660 (0.219)	0.003
H3K27ac[17] + 500bp	0.336	0.557 (0.067)	1.657 (0.198)	0.002
H3K4me1 peaks	0.171	0.394 (0.102)	2.298 (0.593)	0.022
H3K4me1	0.427	0.668 (0.092)	1.565 (0.215)	0.008
H3K4me1 + 500bp	0.609	0.880 (0.052)	1.445 (0.086)	0.000
H3K4me3 peaks	0.042	0.150 (0.055)	3.583 (1.315)	0.061
H3K4me3	0.133	0.219 (0.057)	1.646 (0.425)	0.122
H3K4me3 + 500bp	0.255	0.405 (0.054)	1.585 (0.212)	0.005
H3K9ac peaks	0.039	0.279 (0.056)	7.206 (1.457)	0.000
H3K9ac	0.126	0.214 (0.065)	1.699 (0.519)	0.174
H3K9ac + 500bp	0.231	0.450 (0.051)	1.952 (0.222)	0.000
Intron	0.387	0.424 (0.032)	1.094 (0.083)	0.249
Intron + 500bp	0.397	0.490 (0.030)	1.233 (0.076)	0.002
PromoterFlanking	0.008	0.004 (0.023)	0.477 (2.714)	0.847
PromoterFlanking + 500bp	0.033	0.042 (0.035)	1.262 (1.033)	0.798
Promoter	0.031	0.080 (0.031)	2.559 (0.993)	0.118
Promoter + 500bp	0.039	0.060 (0.024)	1.565 (0.617)	0.359
Repressed	0.461	0.321 (0.104)	0.696 (0.226)	0.174
Repressed + 500bp	0.719	0.619 (0.032)	0.860 (0.045)	0.002
Super Enhancer	0.168	0.217 (0.019)	1.289 (0.115)	0.012
Super Enhancer + 500bp	0.172	0.251 (0.022)	1.464 (0.129)	0.000
TFBS	0.132	0.357 (0.087)	2.692 (0.657)	0.012
TFBS + 500bp	0.343	0.438 (0.071)	1.275 (0.206)	0.186
Transcribed	0.345	0.442 (0.088)	1.280 (0.256)	0.262
Transcribed + 500bp	0.763	0.775 (0.051)	1.015 (0.066)	0.820
TSS	0.018	0.059 (0.030)	3.239 (1.666)	0.181
TSS + 500bp	0.035	0.097 (0.031)	2.792 (0.883)	0.048
3-prime UTR	0.011	0.059 (0.022)	5.352 (2.001)	0.028
3-prime UTR + 500bp	0.027	0.054 (0.021)	2.013 (0.796)	0.206
5-prime UTR	0.005	0.035 (0.018)	6.541 (3.285)	0.094
5-prime UTR + 500bp	0.028	0.055 (0.022)	1.984 (0.794)	0.219
Weak Enhancer	0.021	0.119 (0.039)	5.640 (1.834)	0.010
Weak Enhancer + 500bp	0.089	0.236 (0.044)	2.658 (0.494)	0.001

(b) BMI

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.123 (0.030)	8.413 (2.065)	0.000
Coding + 500bp	0.065	0.094 (0.035)	1.453 (0.538)	0.395
Conserved	0.026	0.462 (0.063)	17.725 (2.423)	0.000
Conserved + 500bp	0.333	0.616 (0.090)	1.853 (0.270)	0.002
CTCF	0.024	0.022 (0.051)	0.935 (2.152)	0.976
CTCF + 500bp	0.071	0.049 (0.053)	0.689 (0.750)	0.677
DGF	0.138	0.207 (0.113)	1.508 (0.824)	0.538
DGF + 500bp	0.542	0.429 (0.084)	0.793 (0.156)	0.182
DHS peaks	0.112	0.008 (0.120)	0.071 (1.073)	0.383
DHS	0.168	0.052 (0.135)	0.311 (0.807)	0.390
DHS + 500bp	0.499	0.631 (0.096)	1.265 (0.193)	0.181
FANTOM5 Enhancer	0.004	-0.000 (0.022)	-0.028 (5.137)	0.841
FANTOM5 Enhancer + 500bp	0.019	0.006 (0.025)	0.321 (1.309)	0.604
Enhancer	0.063	0.137 (0.061)	2.163 (0.960)	0.234
Enhancer + 500bp	0.154	0.215 (0.059)	1.397 (0.384)	0.305
Fetal DHS	0.085	0.108 (0.093)	1.272 (1.101)	0.805
Fetal DHS + 500bp	0.285	0.291 (0.102)	1.020 (0.357)	0.955
H3K27ac[18]	0.391	0.455 (0.037)	1.164 (0.093)	0.083
H3K27ac[18] + 500bp	0.423	0.489 (0.052)	1.158 (0.124)	0.209
H3K27ac[17]	0.269	0.409 (0.071)	1.517 (0.264)	0.051
H3K27ac[17] + 500bp	0.336	0.486 (0.070)	1.446 (0.208)	0.036
H3K4me1 peaks	0.171	0.471 (0.116)	2.747 (0.678)	0.011
H3K4me1	0.427	0.621 (0.086)	1.455 (0.201)	0.028
H3K4me1 + 500bp	0.609	0.847 (0.057)	1.391 (0.094)	0.000
H3K4me3 peaks	0.042	0.211 (0.071)	5.042 (1.694)	0.020
H3K4me3	0.133	0.237 (0.067)	1.779 (0.504)	0.125
H3K4me3 + 500bp	0.255	0.308 (0.064)	1.207 (0.251)	0.414
H3K9ac peaks	0.039	0.220 (0.062)	5.671 (1.594)	0.004
H3K9ac	0.126	0.345 (0.066)	2.736 (0.523)	0.001
H3K9ac + 500bp	0.231	0.460 (0.055)	1.996 (0.238)	0.000
Intron	0.387	0.437 (0.035)	1.129 (0.090)	0.152
Intron + 500bp	0.397	0.537 (0.031)	1.353 (0.078)	0.000
PromoterFlanking	0.008	0.020 (0.031)	2.394 (3.664)	0.704
PromoterFlanking + 500bp	0.033	0.056 (0.033)	1.684 (0.992)	0.490
Promoter	0.031	0.123 (0.033)	3.945 (1.053)	0.005
Promoter + 500bp	0.039	0.116 (0.026)	2.995 (0.661)	0.003
Repressed	0.461	0.385 (0.100)	0.835 (0.216)	0.446
Repressed + 500bp	0.719	0.513 (0.038)	0.714 (0.053)	0.000
Super Enhancer	0.168	0.213 (0.030)	1.264 (0.176)	0.135
Super Enhancer + 500bp	0.172	0.233 (0.029)	1.357 (0.171)	0.040
TFBS	0.132	0.437 (0.098)	3.301 (0.738)	0.003
TFBS + 500bp	0.343	0.427 (0.093)	1.244 (0.270)	0.368
Transcribed	0.345	0.436 (0.086)	1.263 (0.250)	0.288
Transcribed + 500bp	0.763	0.681 (0.058)	0.893 (0.075)	0.156
TSS	0.018	0.165 (0.043)	9.064 (2.357)	0.001
TSS + 500bp	0.035	0.167 (0.036)	4.786 (1.039)	0.000
3-prime UTR	0.011	0.034 (0.022)	3.053 (1.945)	0.295
3-prime UTR + 500bp	0.027	0.047 (0.021)	1.762 (0.765)	0.319
5-prime UTR	0.005	0.042 (0.021)	7.792 (3.845)	0.076
5-prime UTR + 500bp	0.028	0.059 (0.031)	2.129 (1.101)	0.301
Weak Enhancer	0.021	0.011 (0.046)	0.542 (2.157)	0.831
Weak Enhancer + 500bp	0.089	0.113 (0.054)	1.274 (0.603)	0.651

(c) Age at menarche

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.128 (0.093)	8.740 (6.337)	0.224
Coding + 500bp	0.065	0.502 (0.089)	7.782 (1.381)	0.000
Conserved	0.026	0.264 (0.124)	10.111 (4.743)	0.052
Conserved + 500bp	0.333	0.811 (0.142)	2.438 (0.428)	0.001
CTCF	0.024	0.179 (0.109)	7.506 (4.571)	0.140
CTCF + 500bp	0.071	0.079 (0.106)	1.109 (1.494)	0.942
DGF	0.138	0.542 (0.191)	3.938 (1.388)	0.045
DGF + 500bp	0.542	0.806 (0.149)	1.489 (0.275)	0.075
DHS peaks	0.112	0.417 (0.189)	3.730 (1.692)	0.113
DHS	0.168	0.505 (0.247)	3.008 (1.475)	0.167
DHS + 500bp	0.499	0.810 (0.161)	1.623 (0.323)	0.053
FANTOM5 Enhancer	0.004	-0.050 (0.047)	-11.493 (10.765)	0.257
FANTOM5 Enhancer + 500bp	0.019	-0.006 (0.047)	-0.323 (2.442)	0.585
Enhancer	0.063	0.500 (0.157)	7.895 (2.475)	0.007
Enhancer + 500bp	0.154	0.524 (0.120)	3.406 (0.780)	0.003
Fetal DHS	0.085	0.370 (0.194)	4.370 (2.284)	0.122
Fetal DHS + 500bp	0.285	0.783 (0.132)	2.746 (0.462)	0.000
H3K27ac[18]	0.391	0.776 (0.092)	1.984 (0.236)	0.000
H3K27ac[18] + 500bp	0.423	0.962 (0.075)	2.277 (0.177)	0.000
H3K27ac[17]	0.269	0.829 (0.155)	3.075 (0.574)	0.001
H3K27ac[17] + 500bp	0.336	0.772 (0.100)	2.298 (0.299)	0.000
H3K4me1 peaks	0.171	0.430 (0.263)	2.512 (1.536)	0.333
H3K4me1	0.427	1.179 (0.151)	2.765 (0.354)	0.000
H3K4me1 + 500bp	0.609	1.056 (0.094)	1.733 (0.154)	0.000
H3K4me3 peaks	0.042	0.069 (0.186)	1.658 (4.449)	0.881
H3K4me3	0.133	0.628 (0.172)	4.715 (1.292)	0.004
H3K4me3 + 500bp	0.255	0.933 (0.181)	3.652 (0.708)	0.000
H3K9ac peaks	0.039	-0.028 (0.163)	-0.712 (4.213)	0.682
H3K9ac	0.126	0.751 (0.166)	5.951 (1.320)	0.000
H3K9ac + 500bp	0.231	0.832 (0.187)	3.607 (0.812)	0.001
Intron	0.387	0.472 (0.082)	1.218 (0.212)	0.301
Intron + 500bp	0.397	0.657 (0.050)	1.654 (0.127)	0.000
PromoterFlanking	0.008	0.055 (0.073)	6.544 (8.612)	0.504
PromoterFlanking + 500bp	0.033	0.264 (0.087)	7.895 (2.596)	0.013
Promoter	0.031	0.140 (0.073)	4.499 (2.352)	0.126
Promoter + 500bp	0.039	0.173 (0.048)	4.475 (1.243)	0.003
Repressed	0.461	-0.077 (0.140)	-0.167 (0.304)	0.000
Repressed + 500bp	0.719	0.168 (0.077)	0.234 (0.107)	0.000
Super Enhancer	0.168	0.439 (0.059)	2.608 (0.350)	0.000
Super Enhancer + 500bp	0.172	0.467 (0.059)	2.721 (0.343)	0.000
TFBS	0.132	0.871 (0.231)	6.576 (1.742)	0.003
TFBS + 500bp	0.343	0.787 (0.152)	2.291 (0.442)	0.005
Transcribed	0.345	0.573 (0.139)	1.659 (0.403)	0.101
Transcribed + 500bp	0.763	0.627 (0.106)	0.821 (0.139)	0.203
TSS	0.018	0.086 (0.097)	4.746 (5.300)	0.468
TSS + 500bp	0.035	0.452 (0.083)	12.976 (2.372)	0.000
3-prime UTR	0.011	0.035 (0.045)	3.190 (4.093)	0.590
3-prime UTR + 500bp	0.027	0.109 (0.041)	4.044 (1.526)	0.048
5-prime UTR	0.005	0.015 (0.041)	2.768 (7.486)	0.812
5-prime UTR + 500bp	0.028	0.088 (0.069)	3.154 (2.465)	0.380
Weak Enhancer	0.021	0.145 (0.096)	6.876 (4.552)	0.200
Weak Enhancer + 500bp	0.089	0.257 (0.109)	2.890 (1.225)	0.121

(d) LDL

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.058 (0.058)	3.986 (3.940)	0.449
Coding + 500bp	0.065	0.309 (0.064)	4.788 (0.994)	0.000
Conserved	0.026	0.269 (0.075)	10.339 (2.873)	0.001
Conserved + 500bp	0.333	0.582 (0.122)	1.749 (0.366)	0.052
CTCF	0.024	-0.049 (0.068)	-2.077 (2.867)	0.278
CTCF + 500bp	0.071	0.032 (0.084)	0.453 (1.185)	0.641
DGF	0.138	0.093 (0.195)	0.676 (1.420)	0.820
DGF + 500bp	0.542	0.735 (0.149)	1.358 (0.275)	0.184
DHS peaks	0.112	0.219 (0.193)	1.960 (1.726)	0.580
DHS	0.168	0.289 (0.190)	1.721 (1.132)	0.528
DHS + 500bp	0.499	0.921 (0.213)	1.846 (0.428)	0.043
FANTOM5 Enhancer	0.004	0.001 (0.049)	0.162 (11.316)	0.941
FANTOM5 Enhancer + 500bp	0.019	-0.004 (0.051)	-0.213 (2.698)	0.653
Enhancer	0.063	0.211 (0.125)	3.332 (1.972)	0.237
Enhancer + 500bp	0.154	0.512 (0.101)	3.327 (0.659)	0.001
Fetal DHS	0.085	0.091 (0.137)	1.079 (1.617)	0.961
Fetal DHS + 500bp	0.285	0.736 (0.115)	2.583 (0.405)	0.000
H3K27ac^{18}	0.391	0.802 (0.067)	2.051 (0.172)	0.000
H3K27ac^{18} + 500bp	0.423	0.828 (0.072)	1.960 (0.171)	0.000
H3K27ac^{17}	0.269	0.904 (0.190)	3.353 (0.704)	0.001
H3K27ac^{17} + 500bp	0.336	0.839 (0.082)	2.495 (0.244)	0.000
H3K4me1 peaks	0.171	0.602 (0.221)	3.515 (1.289)	0.049
H3K4me1	0.427	1.055 (0.165)	2.474 (0.387)	0.000
H3K4me1 + 500bp	0.609	1.035 (0.093)	1.699 (0.153)	0.000
H3K4me3 peaks	0.042	0.019 (0.129)	0.451 (3.084)	0.859
H3K4me3	0.133	0.530 (0.130)	3.975 (0.972)	0.002
H3K4me3 + 500bp	0.255	0.690 (0.111)	2.702 (0.435)	0.000
H3K9ac peaks	0.039	0.240 (0.121)	6.195 (3.119)	0.107
H3K9ac	0.126	0.632 (0.106)	5.015 (0.842)	0.000
H3K9ac + 500bp	0.231	0.856 (0.110)	3.714 (0.477)	0.000
Intron	0.387	0.523 (0.070)	1.349 (0.180)	0.051
Intron + 500bp	0.397	0.603 (0.048)	1.518 (0.120)	0.000
PromoterFlanking	0.008	-0.039 (0.038)	-4.590 (4.500)	0.225
PromoterFlanking + 500bp	0.033	0.071 (0.058)	2.111 (1.724)	0.513
Promoter	0.031	0.180 (0.073)	5.785 (2.343)	0.041
Promoter + 500bp	0.039	0.162 (0.046)	4.197 (1.187)	0.007
Repressed	0.461	0.143 (0.113)	0.310 (0.246)	0.005
Repressed + 500bp	0.719	0.312 (0.072)	0.434 (0.100)	0.000
Super Enhancer	0.168	0.531 (0.051)	3.151 (0.305)	0.000
Super Enhancer + 500bp	0.172	0.535 (0.048)	3.120 (0.280)	0.000
TFBS	0.132	0.358 (0.189)	2.706 (1.428)	0.236
TFBS + 500bp	0.343	0.601 (0.142)	1.749 (0.412)	0.066
Transcribed	0.345	0.445 (0.108)	1.289 (0.313)	0.346
Transcribed + 500bp	0.763	0.839 (0.070)	1.100 (0.091)	0.278
TSS	0.018	0.066 (0.057)	3.601 (3.138)	0.401
TSS + 500bp	0.035	0.306 (0.072)	8.782 (2.069)	0.000
3-prime UTR	0.011	-0.014 (0.036)	-1.224 (3.300)	0.502
3-prime UTR + 500bp	0.027	0.071 (0.040)	2.623 (1.500)	0.271
5-prime UTR	0.005	0.082 (0.041)	15.172 (7.504)	0.064
5-prime UTR + 500bp	0.028	0.086 (0.039)	3.076 (1.411)	0.139
Weak Enhancer	0.021	0.081 (0.077)	3.859 (3.649)	0.438
Weak Enhancer + 500bp	0.089	0.321 (0.105)	3.605 (1.180)	0.039

(e) HDL

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.052 (0.049)	3.542 (3.317)	0.430
Coding + 500bp	0.065	0.252 (0.051)	3.899 (0.786)	0.000
Conserved	0.026	0.269 (0.080)	10.309 (3.080)	0.001
Conserved + 500bp	0.333	0.664 (0.090)	1.997 (0.272)	0.001
CTCF	0.024	-0.019 (0.079)	-0.814 (3.295)	0.576
CTCF + 500bp	0.071	0.010 (0.077)	0.137 (1.078)	0.415
DGF	0.138	0.237 (0.150)	1.724 (1.092)	0.506
DGF + 500bp	0.542	0.690 (0.108)	1.275 (0.199)	0.164
DHS peaks	0.112	0.145 (0.162)	1.293 (1.448)	0.839
DHS	0.168	0.249 (0.166)	1.484 (0.990)	0.625
DHS + 500bp	0.499	0.941 (0.125)	1.886 (0.250)	0.001
FANTOM5 Enhancer	0.004	-0.047 (0.030)	-10.766 (6.886)	0.090
FANTOM5 Enhancer + 500bp	0.019	0.030 (0.052)	1.551 (2.737)	0.838
Enhancer	0.063	0.232 (0.115)	3.657 (1.814)	0.137
Enhancer + 500bp	0.154	0.559 (0.106)	3.630 (0.685)	0.000
Fetal DHS	0.085	0.333 (0.128)	3.929 (1.511)	0.054
Fetal DHS + 500bp	0.285	0.649 (0.119)	2.276 (0.419)	0.006
H3K27ac[18]	0.391	0.768 (0.060)	1.964 (0.152)	0.000
H3K27ac[18] + 500bp	0.423	0.759 (0.054)	1.797 (0.127)	0.000
H3K27ac[17]	0.269	0.750 (0.149)	2.783 (0.551)	0.002
H3K27ac[17] + 500bp	0.336	0.797 (0.091)	2.373 (0.272)	0.000
H3K4me1 peaks	0.171	0.132 (0.163)	0.772 (0.951)	0.810
H3K4me1	0.427	0.823 (0.144)	1.929 (0.337)	0.006
H3K4me1 + 500bp	0.609	1.181 (0.072)	1.939 (0.119)	0.000
H3K4me3 peaks	0.042	0.121 (0.112)	2.907 (2.685)	0.480
H3K4me3	0.133	0.452 (0.083)	3.394 (0.622)	0.000
H3K4me3 + 500bp	0.255	0.736 (0.104)	2.881 (0.406)	0.000
H3K9ac peaks	0.039	0.172 (0.095)	4.441 (2.450)	0.166
H3K9ac	0.126	0.502 (0.088)	3.978 (0.699)	0.000
H3K9ac + 500bp	0.231	0.751 (0.108)	3.259 (0.469)	0.000
Intron	0.387	0.475 (0.055)	1.225 (0.141)	0.113
Intron + 500bp	0.397	0.550 (0.037)	1.385 (0.094)	0.000
PromoterFlanking	0.008	0.050 (0.043)	5.945 (5.065)	0.335
PromoterFlanking + 500bp	0.033	0.112 (0.060)	3.356 (1.807)	0.184
Promoter	0.031	0.162 (0.052)	5.203 (1.658)	0.015
Promoter + 500bp	0.039	0.153 (0.045)	3.962 (1.161)	0.019
Repressed	0.461	0.081 (0.102)	0.176 (0.222)	0.001
Repressed + 500bp	0.719	0.400 (0.066)	0.556 (0.091)	0.000
Super Enhancer	0.168	0.395 (0.038)	2.346 (0.224)	0.000
Super Enhancer + 500bp	0.172	0.425 (0.035)	2.477 (0.203)	0.000
TFBS	0.132	0.435 (0.159)	3.284 (1.204)	0.060
TFBS + 500bp	0.343	0.545 (0.121)	1.586 (0.353)	0.093
Transcribed	0.345	0.512 (0.097)	1.483 (0.281)	0.098
Transcribed + 500bp	0.763	0.582 (0.097)	0.763 (0.128)	0.075
TSS	0.018	0.065 (0.051)	3.562 (2.802)	0.366
TSS + 500bp	0.035	0.290 (0.058)	8.341 (1.660)	0.000
3-prime UTR	0.011	0.003 (0.037)	0.253 (3.373)	0.824
3-prime UTR + 500bp	0.027	0.057 (0.031)	2.101 (1.152)	0.329
5-prime UTR	0.005	-0.012 (0.025)	-2.291 (4.617)	0.473
5-prime UTR + 500bp	0.028	0.046 (0.035)	1.652 (1.245)	0.598
Weak Enhancer	0.021	0.047 (0.069)	2.237 (3.264)	0.702
Weak Enhancer + 500bp	0.089	0.265 (0.093)	2.982 (1.042)	0.067

(f) Triglycerides

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.074 (0.057)	5.050 (3.916)	0.306
Coding + 500bp	0.065	0.261 (0.068)	4.043 (1.056)	0.003
Conserved	0.026	0.203 (0.096)	7.808 (3.671)	0.067
Conserved + 500bp	0.333	0.568 (0.143)	1.708 (0.431)	0.094
CTCF	0.024	-0.040 (0.105)	-1.659 (4.416)	0.541
CTCF + 500bp	0.071	-0.070 (0.122)	-0.980 (1.718)	0.233
DGF	0.138	0.743 (0.259)	5.402 (1.884)	0.015
DGF + 500bp	0.542	0.860 (0.142)	1.587 (0.263)	0.032
DHS peaks	0.112	0.361 (0.255)	3.229 (2.279)	0.327
DHS	0.168	0.514 (0.266)	3.063 (1.585)	0.190
DHS + 500bp	0.499	0.943 (0.165)	1.891 (0.330)	0.007
FANTOM5 Enhancer	0.004	-0.040 (0.052)	-9.331 (12.109)	0.394
FANTOM5 Enhancer + 500bp	0.019	0.045 (0.064)	2.359 (3.335)	0.681
Enhancer	0.063	0.394 (0.129)	6.217 (2.040)	0.010
Enhancer + 500bp	0.154	0.406 (0.119)	2.635 (0.774)	0.039
Fetal DHS	0.085	0.282 (0.202)	3.324 (2.378)	0.328
Fetal DHS + 500bp	0.285	0.746 (0.166)	2.618 (0.583)	0.007
H3K27ac[18]	0.391	0.727 (0.086)	1.859 (0.220)	0.000
H3K27ac[18] + 500bp	0.423	0.801 (0.083)	1.895 (0.195)	0.000
H3K27ac[17]	0.269	0.639 (0.140)	2.370 (0.521)	0.008
H3K27ac[17] + 500bp	0.336	0.837 (0.128)	2.490 (0.382)	0.000
H3K4me1 peaks	0.171	0.497 (0.198)	2.901 (1.154)	0.103
H3K4me1	0.427	0.783 (0.163)	1.835 (0.383)	0.035
H3K4me1 + 500bp	0.609	1.137 (0.086)	1.866 (0.141)	0.000
H3K4me3 peaks	0.042	0.266 (0.158)	6.363 (3.780)	0.156
H3K4me3	0.133	0.288 (0.127)	2.161 (0.956)	0.229
H3K4me3 + 500bp	0.255	0.890 (0.146)	3.482 (0.573)	0.000
H3K9ac peaks	0.039	0.381 (0.142)	9.820 (3.659)	0.019
H3K9ac	0.126	0.686 (0.140)	5.439 (1.108)	0.000
H3K9ac + 500bp	0.231	0.788 (0.123)	3.418 (0.535)	0.000
Intron	0.387	0.483 (0.066)	1.248 (0.169)	0.129
Intron + 500bp	0.397	0.525 (0.050)	1.323 (0.125)	0.010
PromoterFlanking	0.008	0.001 (0.057)	0.071 (6.760)	0.890
PromoterFlanking + 500bp	0.033	0.108 (0.070)	3.237 (2.104)	0.292
Promoter	0.031	0.104 (0.071)	3.344 (2.279)	0.297
Promoter + 500bp	0.039	0.068 (0.048)	1.765 (1.233)	0.533
Repressed	0.461	0.395 (0.168)	0.856 (0.364)	0.693
Repressed + 500bp	0.719	0.359 (0.074)	0.499 (0.102)	0.000
Super Enhancer	0.168	0.414 (0.054)	2.459 (0.320)	0.000
Super Enhancer + 500bp	0.172	0.415 (0.059)	2.418 (0.342)	0.000
TFBS	0.132	0.364 (0.208)	2.751 (1.569)	0.259
TFBS + 500bp	0.343	0.487 (0.155)	1.418 (0.451)	0.366
Transcribed	0.345	0.302 (0.142)	0.874 (0.411)	0.758
Transcribed + 500bp	0.763	0.677 (0.113)	0.887 (0.148)	0.449
TSS	0.018	0.185 (0.078)	10.152 (4.286)	0.032
TSS + 500bp	0.035	0.141 (0.080)	4.061 (2.305)	0.187
3-prime UTR	0.011	0.055 (0.045)	5.018 (4.095)	0.323
3-prime UTR + 500bp	0.027	0.151 (0.064)	5.624 (2.362)	0.046
5-prime UTR	0.005	-0.003 (0.037)	-0.542 (6.835)	0.821
5-prime UTR + 500bp	0.028	0.029 (0.055)	1.036 (1.990)	0.985
Weak Enhancer	0.021	0.128 (0.091)	6.055 (4.327)	0.241
Weak Enhancer + 500bp	0.089	0.285 (0.112)	3.200 (1.254)	0.084

(g) Coronary artery disease

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.026 (0.070)	1.784 (4.759)	0.869
Coding + 500bp	0.065	0.104 (0.089)	1.614 (1.374)	0.652
Conserved	0.026	0.347 (0.129)	13.300 (4.941)	0.009
Conserved + 500bp	0.333	0.688 (0.177)	2.068 (0.534)	0.039
CTCF	0.024	-0.080 (0.121)	-3.350 (5.058)	0.378
CTCF + 500bp	0.071	0.013 (0.111)	0.182 (1.562)	0.597
DGF	0.138	0.014 (0.328)	0.099 (2.385)	0.706
DGF + 500bp	0.542	1.011 (0.184)	1.867 (0.340)	0.012
DHS peaks	0.112	0.130 (0.303)	1.167 (2.708)	0.951
DHS	0.168	0.385 (0.326)	2.296 (1.943)	0.499
DHS + 500bp	0.499	1.009 (0.172)	2.022 (0.346)	0.006
FANTOM5 Enhancer	0.004	-0.004 (0.055)	-0.922 (12.792)	0.880
FANTOM5 Enhancer + 500bp	0.019	-0.050 (0.070)	-2.628 (3.652)	0.322
Enhancer	0.063	0.258 (0.146)	4.068 (2.303)	0.173
Enhancer + 500bp	0.154	0.503 (0.141)	3.270 (0.914)	0.016
Fetal DHS	0.085	0.208 (0.269)	2.458 (3.180)	0.645
Fetal DHS + 500bp	0.285	0.577 (0.179)	2.025 (0.628)	0.121
H3K27ac^{18}	0.391	0.581 (0.110)	1.485 (0.281)	0.090
H3K27ac^{18} + 500bp	0.423	0.748 (0.107)	1.771 (0.253)	0.003
H3K27ac^{17}	0.269	0.699 (0.190)	2.593 (0.704)	0.023
H3K27ac^{17} + 500bp	0.336	0.760 (0.135)	2.263 (0.403)	0.001
H3K4me1 peaks	0.171	0.586 (0.239)	3.419 (1.394)	0.080
H3K4me1	0.427	0.799 (0.231)	1.873 (0.541)	0.091
H3K4me1 + 500bp	0.609	1.006 (0.102)	1.652 (0.168)	0.000
H3K4me3 peaks	0.042	0.186 (0.152)	4.460 (3.640)	0.333
H3K4me3	0.133	0.517 (0.160)	3.879 (1.197)	0.014
H3K4me3 + 500bp	0.255	0.651 (0.142)	2.549 (0.556)	0.004
H3K9ac peaks	0.039	0.043 (0.174)	1.120 (4.482)	0.979
H3K9ac	0.126	0.632 (0.185)	5.012 (1.465)	0.004
H3K9ac + 500bp	0.231	0.746 (0.147)	3.237 (0.639)	0.000
Intron	0.387	0.526 (0.071)	1.357 (0.183)	0.048
Intron + 500bp	0.397	0.510 (0.055)	1.283 (0.139)	0.043
PromoterFlanking	0.008	0.064 (0.078)	7.616 (9.309)	0.474
PromoterFlanking + 500bp	0.033	0.122 (0.110)	3.631 (3.289)	0.421
Promoter	0.031	0.098 (0.086)	3.132 (2.773)	0.445
Promoter + 500bp	0.039	0.059 (0.054)	1.522 (1.409)	0.710
Repressed	0.461	0.122 (0.229)	0.264 (0.497)	0.136
Repressed + 500bp	0.719	0.380 (0.084)	0.528 (0.116)	0.000
Super Enhancer	0.168	0.307 (0.068)	1.824 (0.406)	0.047
Super Enhancer + 500bp	0.172	0.317 (0.062)	1.850 (0.363)	0.025
TFBS	0.132	0.242 (0.249)	1.827 (1.878)	0.658
TFBS + 500bp	0.343	0.628 (0.184)	1.829 (0.534)	0.132
Transcribed	0.345	0.695 (0.218)	2.013 (0.631)	0.099
Transcribed + 500bp	0.763	0.557 (0.124)	0.730 (0.162)	0.095
TSS	0.018	0.140 (0.088)	7.668 (4.847)	0.159
TSS + 500bp	0.035	0.044 (0.090)	1.276 (2.587)	0.915
3-prime UTR	0.011	-0.021 (0.048)	-1.927 (4.353)	0.500
3-prime UTR + 500bp	0.027	0.020 (0.057)	0.751 (2.108)	0.906
5-prime UTR	0.005	0.077 (0.116)	14.223 (21.357)	0.536
5-prime UTR + 500bp	0.028	0.097 (0.071)	3.480 (2.569)	0.323
Weak Enhancer	0.021	0.143 (0.140)	6.792 (6.656)	0.385
Weak Enhancer + 500bp	0.089	0.280 (0.126)	3.152 (1.422)	0.141

(h) Type 2 Diabetes

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	-0.014 (0.085)	-0.960 (5.796)	0.736
Coding + 500bp	0.065	0.206 (0.087)	3.184 (1.345)	0.108
Conserved	0.026	0.286 (0.119)	10.982 (4.579)	0.025
Conserved + 500bp	0.333	0.874 (0.153)	2.629 (0.461)	0.001
CTCF	0.024	-0.044 (0.117)	-1.842 (4.900)	0.561
CTCF + 500bp	0.071	-0.036 (0.132)	-0.501 (1.860)	0.421
DGF	0.138	0.394 (0.297)	2.861 (2.157)	0.380
DGF + 500bp	0.542	0.723 (0.173)	1.335 (0.320)	0.295
DHS peaks	0.112	0.170 (0.291)	1.523 (2.602)	0.841
DHS	0.168	0.711 (0.307)	4.238 (1.830)	0.075
DHS + 500bp	0.499	0.564 (0.204)	1.132 (0.409)	0.747
FANTOM5 Enhancer	0.004	-0.001 (0.057)	-0.176 (13.241)	0.929
FANTOM5 Enhancer + 500bp	0.019	0.057 (0.072)	2.975 (3.766)	0.601
Enhancer	0.063	0.358 (0.172)	5.658 (2.710)	0.085
Enhancer + 500bp	0.154	0.519 (0.139)	3.370 (0.901)	0.008
Fetal DHS	0.085	0.375 (0.215)	4.424 (2.531)	0.173
Fetal DHS + 500bp	0.285	0.763 (0.206)	2.677 (0.723)	0.020
H3K27ac[18]	0.391	0.679 (0.097)	1.737 (0.247)	0.005
H3K27ac[18] + 500bp	0.423	0.734 (0.096)	1.737 (0.226)	0.003
H3K27ac[17]	0.269	0.734 (0.175)	2.723 (0.649)	0.011
H3K27ac[17] + 500bp	0.336	0.952 (0.159)	2.833 (0.472)	0.000
H3K4me1 peaks	0.171	0.865 (0.281)	5.049 (1.638)	0.007
H3K4me1	0.427	0.743 (0.180)	1.742 (0.422)	0.081
H3K4me1 + 500bp	0.609	1.017 (0.118)	1.670 (0.193)	0.001
H3K4me3 peaks	0.042	-0.014 (0.157)	-0.323 (3.767)	0.725
H3K4me3	0.133	0.583 (0.154)	4.372 (1.157)	0.002
H3K4me3 + 500bp	0.255	0.638 (0.141)	2.496 (0.553)	0.007
H3K9ac peaks	0.039	0.297 (0.153)	7.658 (3.955)	0.092
H3K9ac	0.126	0.753 (0.172)	5.973 (1.366)	0.000
H3K9ac + 500bp	0.231	0.542 (0.150)	2.350 (0.652)	0.052
Intron	0.387	0.596 (0.087)	1.539 (0.224)	0.023
Intron + 500bp	0.397	0.593 (0.064)	1.492 (0.161)	0.001
PromoterFlanking	0.008	-0.075 (0.071)	-8.868 (8.467)	0.236
PromoterFlanking + 500bp	0.033	0.126 (0.084)	3.750 (2.508)	0.267
Promoter	0.031	0.087 (0.080)	2.795 (2.563)	0.489
Promoter + 500bp	0.039	0.163 (0.066)	4.214 (1.720)	0.071
Repressed	0.461	0.326 (0.195)	0.707 (0.423)	0.491
Repressed + 500bp	0.719	0.308 (0.096)	0.429 (0.134)	0.000
Super Enhancer	0.168	0.311 (0.064)	1.848 (0.382)	0.034
Super Enhancer + 500bp	0.172	0.436 (0.064)	2.541 (0.372)	0.000
TFBS	0.132	0.420 (0.229)	3.173 (1.727)	0.209
TFBS + 500bp	0.343	0.497 (0.179)	1.446 (0.521)	0.396
Transcribed	0.345	0.502 (0.187)	1.454 (0.541)	0.398
Transcribed + 500bp	0.763	0.511 (0.139)	0.670 (0.182)	0.060
TSS	0.018	-0.066 (0.085)	-3.643 (4.647)	0.304
TSS + 500bp	0.035	0.113 (0.093)	3.243 (2.665)	0.403
3-prime UTR	0.011	-0.019 (0.053)	-1.722 (4.832)	0.576
3-prime UTR + 500bp	0.027	-0.010 (0.062)	-0.367 (2.316)	0.553
5-prime UTR	0.005	0.041 (0.084)	7.573 (15.429)	0.668
5-prime UTR + 500bp	0.028	0.120 (0.067)	4.312 (2.396)	0.156
Weak Enhancer	0.021	0.210 (0.117)	9.946 (5.569)	0.108
Weak Enhancer + 500bp	0.089	0.313 (0.131)	3.523 (1.472)	0.085

(i) Fasting Glucose

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.085 (0.022)	5.823 (1.494)	0.002
Coding + 500bp	0.065	0.127 (0.026)	1.970 (0.397)	0.015
Conserved	0.026	0.287 (0.044)	11.028 (1.682)	0.000
Conserved + 500bp	0.333	0.658 (0.047)	1.979 (0.140)	0.000
CTCF	0.024	-0.041 (0.032)	-1.716 (1.357)	0.047
CTCF + 500bp	0.071	0.079 (0.033)	1.118 (0.462)	0.799
DGF	0.138	0.168 (0.083)	1.222 (0.602)	0.713
DGF + 500bp	0.542	0.667 (0.057)	1.232 (0.106)	0.034
DHS peaks	0.112	0.066 (0.069)	0.587 (0.622)	0.505
DHS	0.168	0.175 (0.082)	1.045 (0.489)	0.927
DHS + 500bp	0.499	0.687 (0.058)	1.377 (0.115)	0.001
FANTOM5 Enhancer	0.004	-0.024 (0.015)	-5.438 (3.565)	0.071
FANTOM5 Enhancer + 500bp	0.019	-0.001 (0.020)	-0.068 (1.037)	0.304
Enhancer	0.063	0.029 (0.043)	0.465 (0.678)	0.433
Enhancer + 500bp	0.154	0.238 (0.040)	1.544 (0.262)	0.039
Fetal DHS	0.085	0.216 (0.070)	2.547 (0.822)	0.065
Fetal DHS + 500bp	0.285	0.486 (0.060)	1.705 (0.210)	0.001
H3K27ac[18]	0.391	0.503 (0.027)	1.287 (0.070)	0.000
H3K27ac[18] + 500bp	0.423	0.552 (0.036)	1.306 (0.086)	0.001
H3K27ac[17]	0.269	0.372 (0.045)	1.381 (0.169)	0.027
H3K27ac[17] + 500bp	0.336	0.544 (0.042)	1.618 (0.125)	0.000
H3K4me1 peaks	0.171	0.412 (0.072)	2.407 (0.423)	0.001
H3K4me1	0.427	0.646 (0.052)	1.514 (0.123)	0.000
H3K4me1 + 500bp	0.609	0.794 (0.034)	1.304 (0.056)	0.000
H3K4me3 peaks	0.042	0.188 (0.048)	4.511 (1.151)	0.002
H3K4me3	0.133	0.292 (0.046)	2.192 (0.341)	0.001
H3K4me3 + 500bp	0.255	0.353 (0.040)	1.383 (0.155)	0.015
H3K9ac peaks	0.039	0.239 (0.042)	6.163 (1.090)	0.000
H3K9ac	0.126	0.287 (0.051)	2.278 (0.403)	0.002
H3K9ac + 500bp	0.231	0.457 (0.037)	1.981 (0.161)	0.000
Intron	0.387	0.513 (0.024)	1.323 (0.063)	0.000
Intron + 500bp	0.397	0.524 (0.018)	1.321 (0.046)	0.000
PromoterFlanking	0.008	0.029 (0.021)	3.397 (2.541)	0.348
PromoterFlanking + 500bp	0.033	0.070 (0.025)	2.099 (0.756)	0.141
Promoter	0.031	0.068 (0.027)	2.192 (0.882)	0.179
Promoter + 500bp	0.039	0.037 (0.020)	0.952 (0.529)	0.928
Repressed	0.461	0.450 (0.070)	0.975 (0.151)	0.867
Repressed + 500bp	0.719	0.627 (0.027)	0.873 (0.038)	0.001
Super Enhancer	0.168	0.247 (0.022)	1.467 (0.130)	0.001
Super Enhancer + 500bp	0.172	0.253 (0.019)	1.475 (0.114)	0.000
TFBS	0.132	0.217 (0.059)	1.639 (0.448)	0.154
TFBS + 500bp	0.343	0.372 (0.059)	1.083 (0.171)	0.629
Transcribed	0.345	0.391 (0.062)	1.133 (0.179)	0.455
Transcribed + 500bp	0.763	0.812 (0.035)	1.064 (0.046)	0.163
TSS	0.018	0.053 (0.027)	2.918 (1.473)	0.194
TSS + 500bp	0.035	0.107 (0.023)	3.081 (0.666)	0.002
3-prime UTR	0.011	0.062 (0.019)	5.583 (1.699)	0.008
3-prime UTR + 500bp	0.027	0.085 (0.020)	3.140 (0.756)	0.006
5-prime UTR	0.005	0.020 (0.012)	3.656 (2.212)	0.233
5-prime UTR + 500bp	0.028	0.055 (0.020)	1.975 (0.711)	0.173
Weak Enhancer	0.021	0.016 (0.032)	0.759 (1.538)	0.876
Weak Enhancer + 500bp	0.089	0.146 (0.040)	1.643 (0.448)	0.156

(j) Schizophrenia

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.186 (0.090)	12.671 (6.108)	0.053
Coding + 500bp	0.065	0.200 (0.086)	3.098 (1.339)	0.116
Conserved	0.026	0.302 (0.114)	11.588 (4.381)	0.013
Conserved + 500bp	0.333	0.527 (0.115)	1.586 (0.346)	0.095
CTCF	0.024	0.013 (0.112)	0.556 (4.686)	0.925
CTCF + 500bp	0.071	0.138 (0.103)	1.944 (1.454)	0.519
DGF	0.138	0.723 (0.240)	5.251 (1.746)	0.013
DGF + 500bp	0.542	0.854 (0.170)	1.578 (0.315)	0.076
DHS peaks	0.112	0.447 (0.214)	4.001 (1.911)	0.115
DHS	0.168	0.670 (0.254)	3.993 (1.512)	0.044
DHS + 500bp	0.499	0.735 (0.168)	1.474 (0.337)	0.181
FANTOM5 Enhancer	0.004	0.013 (0.047)	2.987 (10.733)	0.853
FANTOM5 Enhancer + 500bp	0.019	-0.106 (0.053)	-5.564 (2.797)	0.015
Enhancer	0.063	0.317 (0.130)	4.999 (2.061)	0.055
Enhancer + 500bp	0.154	0.299 (0.122)	1.940 (0.793)	0.242
Fetal DHS	0.085	0.264 (0.188)	3.120 (2.221)	0.339
Fetal DHS + 500bp	0.285	0.555 (0.170)	1.947 (0.598)	0.123
H3K27ac[18]	0.391	0.456 (0.089)	1.166 (0.228)	0.470
H3K27ac[18] + 500bp	0.423	0.564 (0.086)	1.335 (0.203)	0.097
H3K27ac[17]	0.269	0.574 (0.135)	2.132 (0.502)	0.031
H3K27ac[17] + 500bp	0.336	0.727 (0.116)	2.162 (0.345)	0.001
H3K4me1 peaks	0.171	0.719 (0.217)	4.196 (1.268)	0.012
H3K4me1	0.427	0.970 (0.165)	2.274 (0.386)	0.001
H3K4me1 + 500bp	0.609	0.754 (0.098)	1.238 (0.161)	0.161
H3K4me3 peaks	0.042	0.038 (0.124)	0.905 (2.964)	0.974
H3K4me3	0.133	0.573 (0.147)	4.295 (1.102)	0.002
H3K4me3 + 500bp	0.255	0.220 (0.121)	0.861 (0.475)	0.769
H3K9ac peaks	0.039	0.160 (0.125)	4.124 (3.221)	0.330
H3K9ac	0.126	0.450 (0.152)	3.572 (1.208)	0.032
H3K9ac + 500bp	0.231	0.502 (0.117)	2.176 (0.509)	0.025
Intron	0.387	0.509 (0.091)	1.313 (0.234)	0.176
Intron + 500bp	0.397	0.608 (0.066)	1.531 (0.165)	0.000
PromoterFlanking	0.008	0.051 (0.063)	6.090 (7.510)	0.498
PromoterFlanking + 500bp	0.033	0.081 (0.086)	2.429 (2.555)	0.573
Promoter	0.031	0.140 (0.084)	4.500 (2.703)	0.199
Promoter + 500bp	0.039	0.128 (0.064)	3.317 (1.664)	0.172
Repressed	0.461	0.402 (0.185)	0.871 (0.400)	0.746
Repressed + 500bp	0.719	0.460 (0.068)	0.640 (0.095)	0.000
Super Enhancer	0.168	0.288 (0.047)	1.712 (0.278)	0.014
Super Enhancer + 500bp	0.172	0.252 (0.043)	1.469 (0.251)	0.072
TFBS	0.132	0.459 (0.219)	3.462 (1.651)	0.142
TFBS + 500bp	0.343	0.507 (0.153)	1.477 (0.446)	0.292
Transcribed	0.345	0.311 (0.179)	0.900 (0.518)	0.848
Transcribed + 500bp	0.763	0.773 (0.107)	1.013 (0.141)	0.926
TSS	0.018	0.081 (0.070)	4.435 (3.867)	0.372
TSS + 500bp	0.035	0.244 (0.075)	7.016 (2.141)	0.005
3-prime UTR	0.011	0.094 (0.061)	8.508 (5.543)	0.174
3-prime UTR + 500bp	0.027	0.072 (0.052)	2.664 (1.936)	0.390
5-prime UTR	0.005	0.122 (0.052)	22.400 (9.544)	0.021
5-prime UTR + 500bp	0.028	0.129 (0.052)	4.656 (1.860)	0.047
Weak Enhancer	0.021	0.168 (0.103)	7.988 (4.874)	0.162
Weak Enhancer + 500bp	0.089	0.217 (0.099)	2.435 (1.110)	0.202

(k) Bipolar disorder

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.017 (0.068)	1.145 (4.643)	0.975
Coding + 500bp	0.065	0.140 (0.060)	2.169 (0.923)	0.204
Conserved	0.026	0.186 (0.110)	7.128 (4.207)	0.144
Conserved + 500bp	0.333	0.635 (0.123)	1.910 (0.370)	0.016
CTCF	0.024	0.019 (0.098)	0.802 (4.117)	0.962
CTCF + 500bp	0.071	0.012 (0.107)	0.162 (1.502)	0.575
DGF	0.138	0.257 (0.241)	1.865 (1.751)	0.620
DGF + 500bp	0.542	0.573 (0.145)	1.058 (0.267)	0.828
DHS peaks	0.112	0.041 (0.212)	0.367 (1.898)	0.739
DHS	0.168	-0.021 (0.272)	-0.126 (1.624)	0.487
DHS + 500bp	0.499	0.780 (0.172)	1.564 (0.346)	0.115
FANTOM5 Enhancer	0.004	-0.118 (0.044)	-27.161 (10.077)	0.004
FANTOM5 Enhancer + 500bp	0.019	0.037 (0.049)	1.915 (2.581)	0.725
Enhancer	0.063	0.117 (0.118)	1.852 (1.861)	0.647
Enhancer + 500bp	0.154	0.237 (0.113)	1.537 (0.732)	0.469
Fetal DHS	0.085	0.222 (0.199)	2.618 (2.353)	0.493
Fetal DHS + 500bp	0.285	0.458 (0.170)	1.606 (0.595)	0.322
H3K27ac[18]	0.391	0.528 (0.076)	1.350 (0.195)	0.074
H3K27ac[18] + 500bp	0.423	0.435 (0.089)	1.030 (0.212)	0.888
H3K27ac[17]	0.269	0.362 (0.136)	1.343 (0.503)	0.498
H3K27ac[17] + 500bp	0.336	0.467 (0.116)	1.391 (0.345)	0.256
H3K4me1 peaks	0.171	0.481 (0.215)	2.806 (1.254)	0.148
H3K4me1	0.427	0.867 (0.153)	2.033 (0.358)	0.005
H3K4me1 + 500bp	0.609	0.798 (0.107)	1.309 (0.175)	0.090
H3K4me3 peaks	0.042	0.101 (0.116)	2.424 (2.771)	0.607
H3K4me3	0.133	0.205 (0.123)	1.538 (0.925)	0.561
H3K4me3 + 500bp	0.255	0.277 (0.122)	1.086 (0.477)	0.857
H3K9ac peaks	0.039	-0.025 (0.137)	-0.656 (3.539)	0.641
H3K9ac	0.126	0.244 (0.129)	1.935 (1.021)	0.356
H3K9ac + 500bp	0.231	0.178 (0.122)	0.771 (0.527)	0.662
Intron	0.387	0.417 (0.066)	1.076 (0.170)	0.653
Intron + 500bp	0.397	0.429 (0.055)	1.081 (0.138)	0.557
PromoterFlanking	0.008	0.041 (0.060)	4.904 (7.120)	0.580
PromoterFlanking + 500bp	0.033	0.114 (0.077)	3.412 (2.301)	0.294
Promoter	0.031	0.022 (0.070)	0.692 (2.238)	0.891
Promoter + 500bp	0.039	-0.027 (0.043)	-0.694 (1.125)	0.134
Repressed	0.461	0.402 (0.179)	0.871 (0.389)	0.740
Repressed + 500bp	0.719	0.724 (0.063)	1.006 (0.088)	0.943
Super Enhancer	0.168	0.171 (0.047)	1.017 (0.280)	0.950
Super Enhancer + 500bp	0.172	0.238 (0.045)	1.387 (0.260)	0.140
TFBS	0.132	0.309 (0.179)	2.330 (1.348)	0.327
TFBS + 500bp	0.343	0.386 (0.159)	1.125 (0.462)	0.789
Transcribed	0.345	0.397 (0.158)	1.150 (0.457)	0.741
Transcribed + 500bp	0.763	0.685 (0.113)	0.897 (0.148)	0.489
TSS	0.018	0.078 (0.075)	4.287 (4.092)	0.423
TSS + 500bp	0.035	0.081 (0.062)	2.336 (1.787)	0.455
3-prime UTR	0.011	0.005 (0.040)	0.477 (3.601)	0.884
3-prime UTR + 500bp	0.027	0.052 (0.046)	1.935 (1.725)	0.588
5-prime UTR	0.005	0.001 (0.039)	0.261 (7.130)	0.917
5-prime UTR + 500bp	0.028	0.029 (0.053)	1.041 (1.898)	0.983
Weak Enhancer	0.021	0.126 (0.086)	5.969 (4.064)	0.223
Weak Enhancer + 500bp	0.089	0.139 (0.095)	1.564 (1.066)	0.600

(l) Anorexia

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.103 (0.045)	7.009 (3.057)	0.052
Coding + 500bp	0.065	0.154 (0.053)	2.383 (0.822)	0.093
Conserved	0.026	0.398 (0.075)	15.273 (2.865)	0.000
Conserved + 500bp	0.333	0.785 (0.092)	2.362 (0.276)	0.000
CTCF	0.024	-0.040 (0.062)	-1.658 (2.619)	0.308
CTCF + 500bp	0.071	0.063 (0.076)	0.888 (1.070)	0.916
DGF	0.138	0.065 (0.164)	0.474 (1.192)	0.660
DGF + 500bp	0.542	0.644 (0.112)	1.189 (0.206)	0.365
DHS peaks	0.112	0.346 (0.156)	3.093 (1.393)	0.138
DHS	0.168	0.333 (0.184)	1.985 (1.098)	0.373
DHS + 500bp	0.499	0.995 (0.134)	1.994 (0.270)	0.000
FANTOM5 Enhancer	0.004	0.002 (0.030)	0.406 (6.977)	0.932
FANTOM5 Enhancer + 500bp	0.019	0.074 (0.042)	3.860 (2.193)	0.194
Enhancer	0.063	0.307 (0.085)	4.851 (1.340)	0.004
Enhancer + 500bp	0.154	0.390 (0.088)	2.537 (0.569)	0.008
Fetal DHS	0.085	0.355 (0.146)	4.190 (1.718)	0.066
Fetal DHS + 500bp	0.285	0.870 (0.129)	3.052 (0.453)	0.000
H3K27ac[18]	0.391	0.530 (0.060)	1.354 (0.153)	0.028
H3K27ac[18] + 500bp	0.423	0.468 (0.077)	1.107 (0.183)	0.564
H3K27ac[17]	0.269	0.312 (0.100)	1.157 (0.369)	0.671
H3K27ac[17] + 500bp	0.336	0.480 (0.085)	1.429 (0.253)	0.092
H3K4me1 peaks	0.171	0.602 (0.141)	3.511 (0.822)	0.003
H3K4me1	0.427	0.678 (0.146)	1.589 (0.342)	0.092
H3K4me1 + 500bp	0.609	0.781 (0.076)	1.282 (0.125)	0.032
H3K4me3 peaks	0.042	0.147 (0.095)	3.510 (2.274)	0.265
H3K4me3	0.133	0.358 (0.093)	2.685 (0.699)	0.016
H3K4me3 + 500bp	0.255	0.401 (0.087)	1.569 (0.342)	0.102
H3K9ac peaks	0.039	0.299 (0.084)	7.717 (2.157)	0.001
H3K9ac	0.126	0.442 (0.088)	3.509 (0.696)	0.000
H3K9ac + 500bp	0.231	0.500 (0.076)	2.170 (0.330)	0.000
Intron	0.387	0.471 (0.047)	1.215 (0.122)	0.073
Intron + 500bp	0.397	0.464 (0.037)	1.169 (0.094)	0.066
PromoterFlanking	0.008	0.001 (0.045)	0.073 (5.297)	0.861
PromoterFlanking + 500bp	0.033	0.055 (0.050)	1.636 (1.482)	0.669
Promoter	0.031	0.030 (0.047)	0.973 (1.521)	0.986
Promoter + 500bp	0.039	0.041 (0.035)	1.070 (0.909)	0.939
Repressed	0.461	0.511 (0.141)	1.107 (0.306)	0.726
Repressed + 500bp	0.719	0.498 (0.051)	0.693 (0.071)	0.000
Super Enhancer	0.168	0.188 (0.035)	1.113 (0.206)	0.582
Super Enhancer + 500bp	0.172	0.216 (0.033)	1.259 (0.191)	0.183
TFBS	0.132	0.453 (0.135)	3.420 (1.016)	0.017
TFBS + 500bp	0.343	0.457 (0.130)	1.330 (0.380)	0.391
Transcribed	0.345	0.205 (0.110)	0.594 (0.319)	0.211
Transcribed + 500bp	0.763	0.731 (0.078)	0.958 (0.102)	0.681
TSS	0.018	0.052 (0.048)	2.840 (2.659)	0.491
TSS + 500bp	0.035	0.159 (0.050)	4.558 (1.428)	0.015
3-prime UTR	0.011	0.038 (0.028)	3.478 (2.508)	0.329
3-prime UTR + 500bp	0.027	0.068 (0.033)	2.543 (1.239)	0.217
5-prime UTR	0.005	0.056 (0.033)	10.371 (6.148)	0.131
5-prime UTR + 500bp	0.028	0.132 (0.040)	4.754 (1.439)	0.009
Weak Enhancer	0.021	0.138 (0.069)	6.540 (3.279)	0.095
Weak Enhancer + 500bp	0.089	0.276 (0.072)	3.105 (0.804)	0.010

(m) Years of education

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.116 (0.077)	7.929 (5.251)	0.184
Coding + 500bp	0.065	0.114 (0.076)	1.759 (1.184)	0.520
Conserved	0.026	0.402 (0.126)	15.414 (4.816)	0.003
Conserved + 500bp	0.333	0.750 (0.133)	2.256 (0.401)	0.001
CTCF	0.024	0.095 (0.128)	3.973 (5.379)	0.582
CTCF + 500bp	0.071	0.215 (0.132)	3.029 (1.863)	0.283
DGF	0.138	0.419 (0.285)	3.048 (2.075)	0.318
DGF + 500bp	0.542	0.896 (0.208)	1.655 (0.383)	0.102
DHS peaks	0.112	0.352 (0.268)	3.153 (2.399)	0.370
DHS	0.168	0.433 (0.287)	2.581 (1.710)	0.353
DHS + 500bp	0.499	0.958 (0.204)	1.921 (0.409)	0.032
FANTOM5 Enhancer	0.004	0.006 (0.049)	1.319 (11.412)	0.978
FANTOM5 Enhancer + 500bp	0.019	-0.109 (0.072)	-5.736 (3.797)	0.064
Enhancer	0.063	0.326 (0.151)	5.141 (2.385)	0.081
Enhancer + 500bp	0.154	0.387 (0.166)	2.513 (1.076)	0.170
Fetal DHS	0.085	0.538 (0.241)	6.346 (2.844)	0.060
Fetal DHS + 500bp	0.285	0.808 (0.181)	2.834 (0.634)	0.005
H3K27ac[18]	0.391	0.494 (0.092)	1.263 (0.236)	0.275
H3K27ac[18] + 500bp	0.423	0.379 (0.131)	0.897 (0.310)	0.739
H3K27ac[17]	0.269	0.192 (0.178)	0.713 (0.659)	0.662
H3K27ac[17] + 500bp	0.336	0.549 (0.152)	1.634 (0.453)	0.166
H3K4me1 peaks	0.171	0.643 (0.256)	3.751 (1.494)	0.061
H3K4me1	0.427	0.946 (0.223)	2.218 (0.524)	0.020
H3K4me1 + 500bp	0.609	0.750 (0.135)	1.231 (0.222)	0.313
H3K4me3 peaks	0.042	0.176 (0.181)	4.210 (4.327)	0.463
H3K4me3	0.133	0.275 (0.154)	2.066 (1.154)	0.363
H3K4me3 + 500bp	0.255	0.259 (0.149)	1.016 (0.582)	0.979
H3K9ac peaks	0.039	0.233 (0.153)	6.009 (3.951)	0.209
H3K9ac	0.126	0.252 (0.151)	2.002 (1.193)	0.404
H3K9ac + 500bp	0.231	0.162 (0.146)	0.702 (0.634)	0.635
Intron	0.387	0.372 (0.081)	0.960 (0.210)	0.848
Intron + 500bp	0.397	0.443 (0.068)	1.115 (0.171)	0.499
PromoterFlanking	0.008	-0.017 (0.061)	-1.974 (7.225)	0.682
PromoterFlanking + 500bp	0.033	-0.001 (0.093)	-0.032 (2.786)	0.711
Promoter	0.031	-0.010 (0.070)	-0.334 (2.252)	0.557
Promoter + 500bp	0.039	-0.019 (0.055)	-0.483 (1.414)	0.298
Repressed	0.461	0.192 (0.218)	0.417 (0.472)	0.215
Repressed + 500bp	0.719	0.504 (0.094)	0.701 (0.131)	0.022
Super Enhancer	0.168	0.135 (0.061)	0.800 (0.364)	0.578
Super Enhancer + 500bp	0.172	0.071 (0.062)	0.414 (0.360)	0.093
TFBS	0.132	0.743 (0.244)	5.613 (1.842)	0.016
TFBS + 500bp	0.343	0.385 (0.217)	1.121 (0.630)	0.848
Transcribed	0.345	0.276 (0.197)	0.798 (0.569)	0.723
Transcribed + 500bp	0.763	0.739 (0.113)	0.969 (0.148)	0.834
TSS	0.018	0.065 (0.087)	3.591 (4.775)	0.585
TSS + 500bp	0.035	0.046 (0.080)	1.309 (2.310)	0.894
3-prime UTR	0.011	0.009 (0.053)	0.839 (4.789)	0.973
3-prime UTR + 500bp	0.027	-0.005 (0.054)	-0.171 (2.017)	0.562
5-prime UTR	0.005	-0.009 (0.046)	-1.695 (8.446)	0.750
5-prime UTR + 500bp	0.028	0.029 (0.059)	1.048 (2.110)	0.982
Weak Enhancer	0.021	0.136 (0.116)	6.438 (5.492)	0.321
Weak Enhancer + 500bp	0.089	0.212 (0.128)	2.387 (1.444)	0.345

(n) Ever smoked

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.174 (0.091)	11.891 (6.175)	0.074
Coding + 500bp	0.065	0.365 (0.082)	5.659 (1.264)	0.000
Conserved	0.026	0.109 (0.115)	4.195 (4.394)	0.456
Conserved + 500bp	0.333	0.771 (0.121)	2.319 (0.364)	0.000
CTCF	0.024	-0.006 (0.113)	-0.261 (4.762)	0.790
CTCF + 500bp	0.071	-0.152 (0.113)	-2.140 (1.594)	0.037
DGF	0.138	0.871 (0.252)	6.331 (1.829)	0.003
DGF + 500bp	0.542	1.065 (0.146)	1.966 (0.270)	0.001
DHS peaks	0.112	0.357 (0.255)	3.195 (2.283)	0.327
DHS	0.168	0.523 (0.271)	3.121 (1.613)	0.178
DHS + 500bp	0.499	0.858 (0.145)	1.719 (0.292)	0.020
FANTOM5 Enhancer	0.004	0.158 (0.072)	36.410 (16.504)	0.027
FANTOM5 Enhancer + 500bp	0.019	0.283 (0.084)	14.848 (4.406)	0.002
Enhancer	0.063	0.379 (0.154)	5.984 (2.432)	0.037
Enhancer + 500bp	0.154	0.668 (0.120)	4.342 (0.778)	0.000
Fetal DHS	0.085	0.567 (0.198)	6.690 (2.334)	0.014
Fetal DHS + 500bp	0.285	0.537 (0.157)	1.882 (0.550)	0.122
H3K27ac^{18}	0.391	0.980 (0.086)	2.506 (0.221)	0.000
H3K27ac^{18} + 500bp	0.423	0.957 (0.083)	2.263 (0.195)	0.000
H3K27ac^{17}	0.269	0.951 (0.161)	3.530 (0.597)	0.000
H3K27ac^{17} + 500bp	0.336	0.792 (0.112)	2.358 (0.334)	0.000
H3K4me1 peaks	0.171	0.502 (0.201)	2.931 (1.170)	0.100
H3K4me1	0.427	0.884 (0.190)	2.072 (0.446)	0.017
H3K4me1 + 500bp	0.609	1.041 (0.085)	1.709 (0.140)	0.000
H3K4me3 peaks	0.042	0.313 (0.144)	7.501 (3.444)	0.062
H3K4me3	0.133	0.750 (0.149)	5.628 (1.119)	0.000
H3K4me3 + 500bp	0.255	0.610 (0.124)	2.387 (0.487)	0.004
H3K9ac peaks	0.039	0.146 (0.138)	3.770 (3.571)	0.439
H3K9ac	0.126	0.335 (0.148)	2.655 (1.177)	0.155
H3K9ac + 500bp	0.231	0.434 (0.129)	1.883 (0.561)	0.115
Intron	0.387	0.416 (0.072)	1.073 (0.186)	0.692
Intron + 500bp	0.397	0.513 (0.052)	1.291 (0.132)	0.022
PromoterFlanking	0.008	0.017 (0.073)	2.049 (8.674)	0.903
PromoterFlanking + 500bp	0.033	0.228 (0.096)	6.818 (2.856)	0.044
Promoter	0.031	0.251 (0.079)	8.046 (2.519)	0.007
Promoter + 500bp	0.039	0.169 (0.056)	4.364 (1.442)	0.021
Repressed	0.461	0.179 (0.145)	0.388 (0.315)	0.048
Repressed + 500bp	0.719	0.260 (0.079)	0.362 (0.110)	0.000
Super Enhancer	0.168	0.563 (0.062)	3.341 (0.366)	0.000
Super Enhancer + 500bp	0.172	0.615 (0.060)	3.582 (0.348)	0.000
TFBS	0.132	0.791 (0.221)	5.970 (1.670)	0.002
TFBS + 500bp	0.343	0.552 (0.183)	1.607 (0.532)	0.250
Transcribed	0.345	0.302 (0.144)	0.875 (0.417)	0.764
Transcribed + 500bp	0.763	0.596 (0.104)	0.781 (0.136)	0.111
TSS	0.018	0.341 (0.090)	18.703 (4.964)	0.000
TSS + 500bp	0.035	0.372 (0.080)	10.679 (2.296)	0.000
3-prime UTR	0.011	0.073 (0.047)	6.588 (4.241)	0.190
3-prime UTR + 500bp	0.027	0.107 (0.056)	3.958 (2.062)	0.152
5-prime UTR	0.005	0.019 (0.044)	3.562 (8.057)	0.749
5-prime UTR + 500bp	0.028	0.150 (0.063)	5.381 (2.249)	0.053
Weak Enhancer	0.021	0.230 (0.116)	10.914 (5.504)	0.069
Weak Enhancer + 500bp	0.089	0.424 (0.108)	4.762 (1.217)	0.002

(o) Rheumatoid arthritis

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.125 (0.071)	8.551 (4.849)	0.123
Coding + 500bp	0.065	0.352 (0.065)	5.453 (1.009)	0.000
Conserved	0.026	0.069 (0.072)	2.640 (2.765)	0.545
Conserved + 500bp	0.333	0.919 (0.099)	2.765 (0.296)	0.000
CTCF	0.024	-0.050 (0.086)	-2.081 (3.627)	0.384
CTCF + 500bp	0.071	-0.127 (0.083)	-1.781 (1.168)	0.017
DGF	0.138	0.770 (0.182)	5.600 (1.323)	0.001
DGF + 500bp	0.542	1.088 (0.089)	2.009 (0.165)	0.000
DHS peaks	0.112	0.303 (0.136)	2.713 (1.213)	0.166
DHS	0.168	0.154 (0.177)	0.915 (1.053)	0.936
DHS + 500bp	0.499	0.713 (0.126)	1.430 (0.253)	0.095
FANTOM5 Enhancer	0.004	0.169 (0.042)	39.042 (9.650)	0.000
FANTOM5 Enhancer + 500bp	0.019	0.428 (0.074)	22.468 (3.865)	0.000
Enhancer	0.063	0.237 (0.097)	3.740 (1.529)	0.082
Enhancer + 500bp	0.154	0.554 (0.106)	3.600 (0.690)	0.000
Fetal DHS	0.085	0.398 (0.133)	4.693 (1.571)	0.025
Fetal DHS + 500bp	0.285	0.686 (0.132)	2.406 (0.462)	0.004
H3K27ac[18]	0.391	0.838 (0.049)	2.143 (0.126)	0.000
H3K27ac[18] + 500bp	0.423	0.840 (0.060)	1.987 (0.141)	0.000
H3K27ac[17]	0.269	0.768 (0.121)	2.849 (0.449)	0.000
H3K27ac[17] + 500bp	0.336	0.748 (0.074)	2.227 (0.220)	0.000
H3K4me1 peaks	0.171	0.506 (0.169)	2.953 (0.985)	0.054
H3K4me1	0.427	0.742 (0.132)	1.739 (0.310)	0.017
H3K4me1 + 500bp	0.609	1.004 (0.067)	1.648 (0.111)	0.000
H3K4me3 peaks	0.042	0.318 (0.157)	7.621 (3.764)	0.086
H3K4me3	0.133	0.675 (0.147)	5.064 (1.099)	0.000
H3K4me3 + 500bp	0.255	0.669 (0.126)	2.618 (0.491)	0.001
H3K9ac peaks	0.039	0.082 (0.113)	2.109 (2.923)	0.704
H3K9ac	0.126	0.231 (0.122)	1.834 (0.965)	0.391
H3K9ac + 500bp	0.231	0.565 (0.101)	2.450 (0.437)	0.001
Intron	0.387	0.400 (0.068)	1.032 (0.176)	0.857
Intron + 500bp	0.397	0.504 (0.054)	1.268 (0.135)	0.042
PromoterFlanking	0.008	-0.054 (0.045)	-6.361 (5.290)	0.162
PromoterFlanking + 500bp	0.033	0.018 (0.065)	0.535 (1.955)	0.810
Promoter	0.031	0.146 (0.064)	4.685 (2.051)	0.080
Promoter + 500bp	0.039	0.137 (0.048)	3.553 (1.230)	0.036
Repressed	0.461	0.102 (0.115)	0.222 (0.249)	0.001
Repressed + 500bp	0.719	0.392 (0.052)	0.545 (0.072)	0.000
Super Enhancer	0.168	0.554 (0.050)	3.289 (0.296)	0.000
Super Enhancer + 500bp	0.172	0.594 (0.046)	3.462 (0.268)	0.000
TFBS	0.132	0.614 (0.195)	4.635 (1.470)	0.017
TFBS + 500bp	0.343	0.730 (0.132)	2.126 (0.384)	0.004
Transcribed	0.345	0.402 (0.124)	1.163 (0.360)	0.641
Transcribed + 500bp	0.763	0.747 (0.081)	0.978 (0.106)	0.837
TSS	0.018	0.248 (0.073)	13.613 (4.032)	0.003
TSS + 500bp	0.035	0.398 (0.070)	11.424 (2.013)	0.000
3-prime UTR	0.011	0.021 (0.035)	1.909 (3.157)	0.773
3-prime UTR + 500bp	0.027	0.171 (0.076)	6.347 (2.824)	0.061
5-prime UTR	0.005	0.040 (0.045)	7.436 (8.305)	0.438
5-prime UTR + 500bp	0.028	0.151 (0.047)	5.413 (1.707)	0.015
Weak Enhancer	0.021	0.101 (0.068)	4.797 (3.239)	0.252
Weak Enhancer + 500bp	0.089	0.258 (0.084)	2.903 (0.942)	0.040

(p) Crohn's disease

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.172 (0.088)	11.727 (6.016)	0.071
Coding + 500bp	0.065	0.421 (0.079)	6.529 (1.223)	0.000
Conserved	0.026	0.203 (0.090)	7.786 (3.463)	0.048
Conserved + 500bp	0.333	0.878 (0.123)	2.639 (0.370)	0.000
CTCF	0.024	-0.101 (0.106)	-4.218 (4.448)	0.223
CTCF + 500bp	0.071	-0.077 (0.111)	-1.087 (1.560)	0.174
DGF	0.138	0.901 (0.247)	6.546 (1.797)	0.002
DGF + 500bp	0.542	1.117 (0.134)	2.063 (0.248)	0.000
DHS peaks	0.112	0.706 (0.217)	6.319 (1.943)	0.005
DHS	0.168	0.416 (0.236)	2.481 (1.407)	0.287
DHS + 500bp	0.499	0.815 (0.164)	1.635 (0.330)	0.069
FANTOM5 Enhancer	0.004	0.181 (0.049)	41.783 (11.197)	0.000
FANTOM5 Enhancer + 500bp	0.019	0.285 (0.076)	14.939 (3.999)	0.000
Enhancer	0.063	0.348 (0.135)	5.490 (2.133)	0.035
Enhancer + 500bp	0.154	0.699 (0.138)	4.544 (0.899)	0.000
Fetal DHS	0.085	0.360 (0.186)	4.243 (2.191)	0.147
Fetal DHS + 500bp	0.285	0.550 (0.170)	1.929 (0.597)	0.138
H3K27ac^{18}	0.391	0.989 (0.083)	2.527 (0.213)	0.000
H3K27ac^{18} + 500bp	0.423	1.031 (0.088)	2.440 (0.209)	0.000
H3K27ac^{17}	0.269	0.848 (0.163)	3.148 (0.605)	0.000
H3K27ac^{17} + 500bp	0.336	0.813 (0.133)	2.420 (0.396)	0.000
H3K4me1 peaks	0.171	0.710 (0.243)	4.142 (1.419)	0.029
H3K4me1	0.427	0.774 (0.173)	1.814 (0.406)	0.049
H3K4me1 + 500bp	0.609	0.911 (0.078)	1.495 (0.128)	0.001
H3K4me3 peaks	0.042	0.264 (0.174)	6.318 (4.164)	0.207
H3K4me3	0.133	0.709 (0.179)	5.321 (1.345)	0.001
H3K4me3 + 500bp	0.255	0.707 (0.137)	2.767 (0.536)	0.003
H3K9ac peaks	0.039	0.276 (0.144)	7.125 (3.713)	0.102
H3K9ac	0.126	0.584 (0.172)	4.634 (1.365)	0.010
H3K9ac + 500bp	0.231	0.692 (0.122)	3.002 (0.531)	0.000
Intron	0.387	0.364 (0.082)	0.941 (0.211)	0.777
Intron + 500bp	0.397	0.506 (0.055)	1.275 (0.138)	0.055
PromoterFlanking	0.008	0.030 (0.055)	3.586 (6.533)	0.693
PromoterFlanking + 500bp	0.033	0.049 (0.080)	1.464 (2.381)	0.845
Promoter	0.031	0.150 (0.072)	4.799 (2.305)	0.110
Promoter + 500bp	0.039	0.185 (0.054)	4.797 (1.390)	0.004
Repressed	0.461	0.065 (0.160)	0.140 (0.346)	0.014
Repressed + 500bp	0.719	0.275 (0.072)	0.383 (0.100)	0.000
Super Enhancer	0.168	0.567 (0.062)	3.365 (0.367)	0.000
Super Enhancer + 500bp	0.172	0.616 (0.057)	3.593 (0.330)	0.000
TFBS	0.132	1.144 (0.282)	8.637 (2.133)	0.001
TFBS + 500bp	0.343	0.660 (0.173)	1.921 (0.503)	0.070
Transcribed	0.345	0.446 (0.163)	1.291 (0.471)	0.527
Transcribed + 500bp	0.763	0.677 (0.106)	0.888 (0.139)	0.420
TSS	0.018	0.209 (0.065)	11.447 (3.561)	0.004
TSS + 500bp	0.035	0.307 (0.076)	8.827 (2.189)	0.000
3-prime UTR	0.011	0.034 (0.053)	3.111 (4.774)	0.655
3-prime UTR + 500bp	0.027	0.176 (0.065)	6.524 (2.423)	0.023
5-prime UTR	0.005	0.097 (0.043)	17.831 (7.966)	0.033
5-prime UTR + 500bp	0.028	0.204 (0.073)	7.325 (2.617)	0.026
Weak Enhancer	0.021	0.057 (0.099)	2.723 (4.685)	0.712
Weak Enhancer + 500bp	0.089	0.328 (0.106)	3.690 (1.191)	0.022

(q) Ulcerative colitis

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.123 (0.052)	8.410 (3.529)	0.042
Coding + 500bp	0.065	0.119 (0.057)	1.846 (0.883)	0.340
Conserved	0.026	0.404 (0.085)	15.497 (3.251)	0.000
Conserved + 500bp	0.333	0.797 (0.098)	2.397 (0.296)	0.000
CTCF	0.024	0.006 (0.072)	0.266 (3.040)	0.809
CTCF + 500bp	0.071	0.050 (0.084)	0.700 (1.185)	0.799
DGF	0.138	0.050 (0.184)	0.360 (1.337)	0.632
DGF + 500bp	0.542	0.540 (0.130)	0.997 (0.239)	0.989
DHS peaks	0.112	0.099 (0.170)	0.886 (1.519)	0.940
DHS	0.168	0.194 (0.203)	1.158 (1.207)	0.896
DHS + 500bp	0.499	1.105 (0.140)	2.215 (0.280)	0.000
FANTOM5 Enhancer	0.004	0.034 (0.032)	7.781 (7.318)	0.354
FANTOM5 Enhancer + 500bp	0.019	0.148 (0.055)	7.754 (2.901)	0.018
Enhancer	0.063	0.132 (0.099)	2.082 (1.564)	0.488
Enhancer + 500bp	0.154	0.374 (0.099)	2.427 (0.643)	0.030
Fetal DHS	0.085	0.319 (0.143)	3.760 (1.688)	0.103
Fetal DHS + 500bp	0.285	0.884 (0.136)	3.103 (0.476)	0.000
H3K27ac[18]	0.391	0.474 (0.059)	1.211 (0.150)	0.166
H3K27ac[18] + 500bp	0.423	0.447 (0.080)	1.057 (0.189)	0.763
H3K27ac[17]	0.269	0.268 (0.107)	0.993 (0.397)	0.986
H3K27ac[17] + 500bp	0.336	0.450 (0.096)	1.340 (0.285)	0.238
H3K4me1 peaks	0.171	0.463 (0.167)	2.704 (0.977)	0.078
H3K4me1	0.427	0.709 (0.144)	1.662 (0.337)	0.052
H3K4me1 + 500bp	0.609	0.721 (0.079)	1.184 (0.129)	0.166
H3K4me3 peaks	0.042	0.122 (0.106)	2.916 (2.535)	0.445
H3K4me3	0.133	0.378 (0.096)	2.832 (0.722)	0.009
H3K4me3 + 500bp	0.255	0.391 (0.102)	1.529 (0.397)	0.181
H3K9ac peaks	0.039	0.338 (0.104)	8.710 (2.685)	0.003
H3K9ac	0.126	0.450 (0.103)	3.568 (0.817)	0.002
H3K9ac + 500bp	0.231	0.412 (0.091)	1.785 (0.393)	0.042
Intron	0.387	0.436 (0.052)	1.125 (0.134)	0.342
Intron + 500bp	0.397	0.475 (0.040)	1.196 (0.100)	0.044
PromoterFlanking	0.008	0.057 (0.052)	6.773 (6.187)	0.347
PromoterFlanking + 500bp	0.033	0.088 (0.055)	2.634 (1.638)	0.315
Promoter	0.031	0.065 (0.065)	2.093 (2.082)	0.598
Promoter + 500bp	0.039	0.023 (0.041)	0.597 (1.060)	0.703
Repressed	0.461	0.393 (0.147)	0.852 (0.319)	0.640
Repressed + 500bp	0.719	0.546 (0.058)	0.759 (0.081)	0.003
Super Enhancer	0.168	0.214 (0.038)	1.269 (0.226)	0.239
Super Enhancer + 500bp	0.172	0.213 (0.040)	1.243 (0.236)	0.309
TFBS	0.132	0.285 (0.133)	2.152 (1.002)	0.252
TFBS + 500bp	0.343	0.494 (0.154)	1.438 (0.450)	0.329
Transcribed	0.345	0.330 (0.128)	0.955 (0.371)	0.905
Transcribed + 500bp	0.763	0.691 (0.093)	0.906 (0.121)	0.439
TSS	0.018	0.055 (0.052)	3.025 (2.838)	0.476
TSS + 500bp	0.035	0.185 (0.052)	5.314 (1.496)	0.005
3-prime UTR	0.011	0.025 (0.035)	2.299 (3.173)	0.683
3-prime UTR + 500bp	0.027	0.045 (0.039)	1.668 (1.435)	0.643
5-prime UTR	0.005	0.068 (0.037)	12.546 (6.780)	0.091
5-prime UTR + 500bp	0.028	0.152 (0.048)	5.450 (1.733)	0.011
Weak Enhancer	0.021	0.062 (0.077)	2.920 (3.667)	0.600
Weak Enhancer + 500bp	0.089	0.299 (0.084)	3.357 (0.940)	0.015

(r) Went to college (yes/no)

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.095 (0.066)	6.501 (4.510)	0.234
Coding + 500bp	0.065	0.453 (0.073)	7.018 (1.126)	0.000
Conserved	0.026	0.178 (0.091)	6.834 (3.494)	0.100
Conserved + 500bp	0.333	0.777 (0.110)	2.335 (0.331)	0.000
CTCF	0.024	0.068 (0.090)	2.834 (3.795)	0.625
CTCF + 500bp	0.071	0.022 (0.095)	0.310 (1.339)	0.595
DGF	0.138	0.425 (0.191)	3.090 (1.390)	0.137
DGF + 500bp	0.542	0.747 (0.097)	1.379 (0.179)	0.043
DHS peaks	0.112	0.264 (0.191)	2.362 (1.713)	0.431
DHS	0.168	0.417 (0.226)	2.488 (1.349)	0.273
DHS + 500bp	0.499	0.863 (0.133)	1.731 (0.267)	0.011
FANTOM5 Enhancer	0.004	-0.042 (0.038)	-9.708 (8.772)	0.240
FANTOM5 Enhancer + 500bp	0.019	0.033 (0.047)	1.731 (2.474)	0.763
Enhancer	0.063	0.352 (0.126)	5.561 (1.997)	0.023
Enhancer + 500bp	0.154	0.556 (0.101)	3.612 (0.654)	0.000
Fetal DHS	0.085	0.182 (0.167)	2.146 (1.970)	0.557
Fetal DHS + 500bp	0.285	0.653 (0.117)	2.290 (0.412)	0.006
H3K27ac[18]	0.391	0.809 (0.073)	2.069 (0.186)	0.000
H3K27ac[18] + 500bp	0.423	0.962 (0.062)	2.277 (0.147)	0.000
H3K27ac[17]	0.269	0.933 (0.203)	3.461 (0.752)	0.003
H3K27ac[17] + 500bp	0.336	0.867 (0.081)	2.579 (0.240)	0.000
H3K4me1 peaks	0.171	0.534 (0.241)	3.117 (1.408)	0.148
H3K4me1	0.427	1.092 (0.126)	2.560 (0.295)	0.000
H3K4me1 + 500bp	0.609	1.051 (0.060)	1.726 (0.099)	0.000
H3K4me3 peaks	0.042	-0.014 (0.149)	-0.332 (3.563)	0.704
H3K4me3	0.133	0.523 (0.128)	3.926 (0.963)	0.003
H3K4me3 + 500bp	0.255	0.948 (0.145)	3.711 (0.566)	0.000
H3K9ac peaks	0.039	-0.151 (0.167)	-3.886 (4.312)	0.247
H3K9ac	0.126	0.522 (0.139)	4.143 (1.103)	0.004
H3K9ac + 500bp	0.231	0.972 (0.173)	4.217 (0.749)	0.000
Intron	0.387	0.486 (0.059)	1.254 (0.153)	0.089
Intron + 500bp	0.397	0.626 (0.045)	1.576 (0.113)	0.000
PromoterFlanking	0.008	-0.009 (0.055)	-1.042 (6.491)	0.752
PromoterFlanking + 500bp	0.033	0.230 (0.085)	6.877 (2.540)	0.024
Promoter	0.031	0.144 (0.057)	4.623 (1.815)	0.045
Promoter + 500bp	0.039	0.164 (0.041)	4.257 (1.061)	0.002
Repressed	0.461	-0.048 (0.116)	-0.105 (0.251)	0.000
Repressed + 500bp	0.719	0.261 (0.066)	0.363 (0.091)	0.000
Super Enhancer	0.168	0.454 (0.056)	2.697 (0.335)	0.000
Super Enhancer + 500bp	0.172	0.481 (0.053)	2.802 (0.311)	0.000
TFBS	0.132	0.708 (0.196)	5.347 (1.478)	0.007
TFBS + 500bp	0.343	0.666 (0.121)	1.939 (0.352)	0.008
Transcribed	0.345	0.562 (0.111)	1.627 (0.320)	0.057
Transcribed + 500bp	0.763	0.700 (0.093)	0.918 (0.122)	0.492
TSS	0.018	0.054 (0.078)	2.938 (4.295)	0.648
TSS + 500bp	0.035	0.431 (0.093)	12.374 (2.679)	0.000
3-prime UTR	0.011	0.030 (0.035)	2.722 (3.160)	0.583
3-prime UTR + 500bp	0.027	0.108 (0.037)	4.008 (1.362)	0.030
5-prime UTR	0.005	0.000 (0.035)	0.023 (6.478)	0.878
5-prime UTR + 500bp	0.028	0.108 (0.058)	3.883 (2.074)	0.167
Weak Enhancer	0.021	0.123 (0.093)	5.823 (4.391)	0.282
Weak Enhancer + 500bp	0.089	0.289 (0.101)	3.251 (1.134)	0.055

(s) Total cholesterol

Supplementary Table 5: Proportion of heritability and enrichment for different functional categories for 17 traits.

Annotation	Prop. SNPs	Prop. h^2	Enrichment	Enrichment P-value
Coding	0.015	0.108 (0.013)	7.359 (0.861)	0.000
Coding + 500bp	0.065	0.192 (0.030)	2.978 (0.469)	0.000
Conserved	0.026	0.359 (0.042)	13.758 (1.606)	0.000
Conserved + 500bp	0.333	0.656 (0.026)	1.972 (0.079)	0.000
CTCF	0.024	-0.013 (0.019)	-0.566 (0.810)	0.256
CTCF + 500bp	0.071	0.043 (0.020)	0.599 (0.279)	0.148
DGF	0.138	0.367 (0.097)	2.667 (0.702)	0.018
DGF + 500bp	0.542	0.748 (0.071)	1.381 (0.132)	0.005
DHS peaks	0.112	0.221 (0.065)	1.976 (0.584)	0.073
DHS	0.168	0.279 (0.070)	1.665 (0.420)	0.098
DHS + 500bp	0.499	0.756 (0.040)	1.515 (0.081)	0.000
FANTOM5 Enhancer	0.004	-0.004 (0.009)	-0.853 (2.158)	0.507
FANTOM5 Enhancer + 500bp	0.019	0.016 (0.018)	0.817 (0.920)	0.686
Enhancer	0.063	0.242 (0.051)	3.828 (0.811)	0.000
Enhancer + 500bp	0.154	0.349 (0.043)	2.266 (0.280)	0.000
Fetal DHS	0.085	0.237 (0.044)	2.791 (0.518)	0.001
Fetal DHS + 500bp	0.285	0.558 (0.059)	1.958 (0.207)	0.000
H3K27ac[18]	0.391	0.627 (0.055)	1.604 (0.141)	0.000
H3K27ac[18] + 500bp	0.423	0.664 (0.060)	1.571 (0.142)	0.000
H3K27ac[17]	0.269	0.485 (0.056)	1.799 (0.207)	0.000
H3K27ac[17] + 500bp	0.336	0.607 (0.042)	1.807 (0.124)	0.000
H3K4me1 peaks	0.171	0.464 (0.041)	2.710 (0.242)	0.000
H3K4me1	0.427	0.807 (0.066)	1.891 (0.156)	0.000
H3K4me1 + 500bp	0.609	0.899 (0.041)	1.476 (0.067)	0.000
H3K4me3 peaks	0.042	0.166 (0.026)	3.961 (0.619)	0.000
H3K4me3	0.133	0.345 (0.045)	2.590 (0.335)	0.000
H3K4me3 + 500bp	0.255	0.488 (0.058)	1.909 (0.227)	0.000
H3K9ac peaks	0.039	0.259 (0.025)	6.671 (0.636)	0.000
H3K9ac	0.126	0.409 (0.057)	3.241 (0.452)	0.000
H3K9ac + 500bp	0.231	0.502 (0.041)	2.178 (0.178)	0.000
Intron	0.387	0.467 (0.014)	1.206 (0.035)	0.004
Intron + 500bp	0.397	0.528 (0.015)	1.329 (0.037)	0.000
PromoterFlanking	0.008	0.010 (0.011)	1.136 (1.347)	0.974
PromoterFlanking + 500bp	0.033	0.083 (0.018)	2.488 (0.544)	0.020
Promoter	0.031	0.091 (0.016)	2.923 (0.522)	0.006
Promoter + 500bp	0.039	0.079 (0.017)	2.043 (0.441)	0.023
Repressed	0.461	0.268 (0.065)	0.580 (0.141)	0.004
Repressed + 500bp	0.719	0.443 (0.049)	0.616 (0.069)	0.000
Super Enhancer	0.168	0.303 (0.036)	1.796 (0.214)	0.000
Super Enhancer + 500bp	0.172	0.316 (0.038)	1.843 (0.221)	0.000
TFBS	0.132	0.440 (0.065)	3.320 (0.491)	0.000
TFBS + 500bp	0.343	0.481 (0.054)	1.400 (0.156)	0.016
Transcribed	0.345	0.430 (0.039)	1.244 (0.112)	0.108
Transcribed + 500bp	0.763	0.726 (0.028)	0.952 (0.037)	0.166
TSS	0.018	0.105 (0.024)	5.770 (1.306)	0.001
TSS + 500bp	0.035	0.171 (0.029)	4.915 (0.842)	0.000
3-prime UTR	0.011	0.053 (0.010)	4.781 (0.873)	0.007
3-prime UTR + 500bp	0.027	0.075 (0.011)	2.793 (0.422)	0.003
5-prime UTR	0.005	0.029 (0.008)	5.305 (1.404)	0.007
5-prime UTR + 500bp	0.028	0.067 (0.011)	2.395 (0.385)	0.001
Weak Enhancer	0.021	0.070 (0.024)	3.328 (1.141)	0.002
Weak Enhancer + 500bp	0.089	0.190 (0.030)	2.138 (0.343)	0.000
$0.0 < DAF < 0.1$	0.175	0.071 (0.009)	0.408 (0.054)	0.000
$0.1 < DAF < 0.2$	0.211	0.215 (0.013)	1.021 (0.063)	0.811
$0.2 < DAF < 0.3$	0.144	0.143 (0.019)	0.994 (0.132)	0.836
$0.3 < DAF < 0.4$	0.111	0.142 (0.023)	1.284 (0.211)	0.192
$0.4 < DAF < 0.6$	0.161	0.223 (0.012)	1.387 (0.073)	0.000
$0.6 < DAF < 0.8$	0.116	0.175 (0.027)	1.514 (0.235)	0.019

Supplementary Table 6: Proportion of heritability and enrichment for different functional categories, meta-analyzed over nine traits, including derived allele frequency bins in the model (Online Methods).

Cell type	cell-type group	Mark	$-log_{10}(p)$
Chondrogenic dif**	Connective/Bone	H3K27ac	6.81
Penis foreskin fibroblast primary**	Connective/Bone	H3K4me1	6.43
Fetal lung**	Cardiovascular	H3K4me1	6.34
Fetal stomach**	GI	H3K4me1	5.48
Colon smooth muscle*	GI	H3K4me1	4.64
Aorta*	Cardiovascular	H3K4me3	4.64
Fetal lung*	Cardiovascular	H3K9ac	4.31
Stomach smooth muscle*	GI	H3K4me3	4.26
Osteoblast*	Connective/Bone	H3K27ac	4.04
Penis foreskin fibroblast primary*	Connective/Bone	H3K4me3	3.96
Stomach smooth muscle*	GI	H3K4me1	3.94
Fetal leg muscle*	Skeletal Muscle	H3K4me3	3.91
Fetal trunk muscle*	Skeletal Muscle	H3K4me3	3.72
Rectal smooth muscle*	GI	H3K4me3	3.57
Fetal lung*	Cardiovascular	H3K4me3	3.37
Rectal smooth muscle*	GI	H3K4me1	3.32
Fetal placenta*	Other	H3K4me3	3.26
Adipose nuclei*	Other	H3K4me1	3.1
Ovary*	Other	H3K4me1	3.06
Fetal large intestine*	GI	H3K4me3	3.05
Placenta chorion*	Other	H3K4me3	2.98
CD34 primary*	Immune	H3K4me1	2.96
Penis foreskin melanocyte primary*	Other	H3K4me1	2.95
Skeletal muscle*	Skeletal Muscle	H3K9ac	2.93
Mobilized CD34 primary*	Immune	H3K4me1	2.88
Fetal stomach*	GI	H3K4me3	2.87
Mobilized CD34 primary*	Immune	H3K4me3	2.87
Fetal adrenal*	Adrenal/Pancreas	H3K4me3	2.86
Breast fibroblast primary*	Connective/Bone	H3K4me3	2.85
Duodenum smooth muscle*	GI	H3K4me1	2.81
Colon smooth muscle*	GI	H3K4me3	2.76
Ovary*	Other	H3K4me3	2.7
Fetal brain*	CNS	H3K4me3	2.62
Skeletal muscle*	Skeletal Muscle	H3K4me1	2.6
Fetal small intestine*	GI	H3K4me3	2.6
Colon smooth muscle*	GI	H3K27ac	2.57
Lung*	Cardiovascular	H3K4me3	2.56
Liver (UCSD)*	Liver	H3K4me3	2.53
Esophagus*	GI	H3K4me3	2.53
Placenta amnion*	Other	H3K4me3	2.48
Right ventricle*	Cardiovascular	H3K4me3	2.47
Sigmoid colon*	GI	H3K4me3	2.44
Fetal leg muscle*	Skeletal Muscle	H3K4me1	2.44
Colonic mucosa*	GI	H3K4me3	2.18
Right atrium*	Cardiovascular	H3K4me3	2.14
CD34 primary*	Immune	H3K4me3	2.13
Gastric*	GI	H3K4me3	2.08
Skeletal muscle*	Skeletal Muscle	H3K4me3	2.07
Lung*	Cardiovascular	H3K4me1	2.06
Pancreatic islets*	Adrenal/Pancreas	H3K4me3	2.05
Adipose nuclei*	Other	H3K9ac	2.01
Right atrium*	Cardiovascular	H3K4me1	1.98
Stomach smooth muscle*	GI	H3K27ac	1.96
Rectal smooth muscle*	GI	H3K27ac	1.95
Breast fibroblast primary*	Connective/Bone	H3K4me1	1.93
Germinal matrix*	CNS	H3K4me3	1.92
Small intestine*	GI	H3K4me3	1.91
Fetal placenta*	Other	H3K4me1	1.91

(a) Height

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Fetal brain*	CNS	H3K4me3	4.48
Penis foreskin fibroblast primary*	Connective/Bone	H3K4me3	4.43
Inferior temporal lobe*	CNS	H3K4me1	4.3
Mid frontal lobe*	CNS	H3K9ac	4.25
Anterior caudate*	CNS	H3K4me3	4.25
Mid frontal lobe*	CNS	H3K27ac	3.96
Anterior caudate*	CNS	H3K9ac	3.91
Cingulate gyrus*	CNS	H3K4me1	3.73
Inferior temporal lobe*	CNS	H3K4me3	3.73
Penis foreskin keratinocyte primary*	Other	H3K9ac	3.72
Mid frontal lobe*	CNS	H3K4me3	3.71
Hippocampus middle*	CNS	H3K4me1	3.66
Inferior temporal lobe*	CNS	H3K9ac	3.59
Fetal brain*	CNS	H3K9ac	3.57
Hippocampus middle*	CNS	H3K9ac	3.47
Cingulate gyrus*	CNS	H3K9ac	3.46
Hippocampus middle*	CNS	H3K4me3	3.4
Germinal matrix*	CNS	H3K4me3	3.4
Cingulate gyrus*	CNS	H3K4me3	3.4
Anterior caudate*	CNS	H3K4me1	3.31
Substantia nigra*	CNS	H3K4me3	3.24
Angular gyrus*	CNS	H3K27ac	3.05
Penis foreskin melanocyte primary*	Other	H3K4me3	2.83
Angular gyrus*	CNS	H3K4me3	2.76
Substantia nigra*	CNS	H3K4me1	2.75
Pancreatic islets*	Adrenal/Pancreas	H3K4me3	2.6
Cingulate gyrus*	CNS	H3K27ac	2.57
Fetal adrenal*	Adrenal/Pancreas	H3K4me3	2.57
Angular gyrus*	CNS	H3K9ac	2.51
Inferior temporal lobe*	CNS	H3K27ac	2.39
Breast myoepithelial*	Other	H3K4me3	2.35
Substantia nigra*	CNS	H3K9ac	2.26
Substantia nigra*	CNS	H3K27ac	2.22
Hippocampus middle*	CNS	H3K27ac	2.07

(b) BMI

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Fetal brain**	CNS	H3K4me3	12.25
Pancreatic islets**	Adrenal/Pancreas	H3K4me3	11.73
Angular gyrus**	CNS	H3K4me3	11.22
Germinal matrix**	CNS	H3K4me3	11.18
Fetal adrenal**	Adrenal/Pancreas	H3K4me3	11.12
Mid frontal lobe**	CNS	H3K4me3	11.11
Inferior temporal lobe**	CNS	H3K4me3	10.22
Cingulate gyrus**	CNS	H3K4me3	9.94
Anterior caudate**	CNS	H3K4me3	8.91
Psoas muscle**	Skeletal Muscle	H3K4me3	8.66
Right ventricle**	Cardiovascular	H3K4me3	8.58
Pancreatic islets**	Adrenal/Pancreas	H3K9ac	7.74
Fetal leg muscle**	Skeletal Muscle	H3K4me3	7.71
Pancreas**	Adrenal/Pancreas	H3K4me3	7.26
Hippocampus middle**	CNS	H3K4me3	7.19
Breast myoepithelial**	Other	H3K4me3	6.93
Fetal trunk muscle**	Skeletal Muscle	H3K4me3	6.87
Peripheralblood mononuclear primary**	Immune	H3K4me3	6.66
Penis foreskin melanocyte primary**	Other	H3K4me3	6.53
Fetal stomach**	GI	H3K4me3	6.26
Gastric**	GI	H3K4me3	6.24
Right atrium**	Cardiovascular	H3K4me3	6.24
CD4+ CD25- CD45RA+ naive primary**	Immune	H3K4me3	6.16
CD4+ CD25int CD127+ Tmem primary**	Immune	H3K4me3	5.96
Ovary**	Other	H3K4me3	5.64
Penis foreskin fibroblast primary**	Connective/Bone	H3K4me3	5.57
Substantia nigra**	CNS	H3K4me3	5.41
Esophagus**	GI	H3K4me3	5.35
Colonic mucosa**	GI	H3K4me3	5.3
Fetal large intestine**	GI	H3K4me3	5.14
Fetal placenta**	Other	H3K4me3	5.07
Fetal brain**	CNS	H3K9ac	5.05
Aorta*	Cardiovascular	H3K4me3	4.74
CD8 naive primary (BI)*	Immune	H3K4me3	4.49
CD14 primary*	Immune	H3K4me3	4.49
Fetal small intestine*	GI	H3K4me3	4.43
Breast vHMEC*	Other	H3K4me3	4.39
CD4+ CD25- Th primary*	Immune	H3K4me3	4.38
CD34 primary*	Immune	H3K4me3	4.37
Placenta amnion*	Other	H3K4me3	4.34
Angular gyrus*	CNS	H3K9ac	4.33
Penis foreskin keratinocyte primary*	Other	H3K4me3	4.3
Pancreatic islets*	Adrenal/Pancreas	H3K4me3	4.26
Mid frontal lobe*	CNS	H3K9ac	4.23
CD4+ CD25- CD45R0+ memory primary*	Immune	H3K4me3	4.14
Rectal smooth muscle*	GI	H3K4me3	4.12
Left Ventricle*	Cardiovascular	H3K4me3	4.11
CD8 memory primary*	Immune	H3K4me3	4.06
CD4+ CD25+ CD127- Treg primary*	Immune	H3K4me3	4.05
Placenta chorion*	Other	H3K4me3	4.05
CD8 naive primary (UCSF-UBC)*	Immune	H3K4me3	3.77
Anterior caudate*	CNS	H3K9ac	3.73
Cingulate gyrus*	CNS	H3K9ac	3.69
CD19 primary (UW)*	Immune	H3K4me3	3.63
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary*	Immune	H3K4me3	3.58
CD4 naive primary*	Immune	H3K4me3	3.53
Fetal brain*	CNS	H3K4me3	3.53
Lung*	Cardiovascular	H3K4me3	3.5
Mid frontal lobe*	CNS	H3K27ac	3.43
Breast fibroblast primary*	Connective/Bone	H3K4me3	3.41

(c) Age at menarche

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at p < 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Liver (BI)*	Liver	H3K4me1	4.76
Fetal adrenal*	Adrenal/Pancreas	H3K4me1	3.41
CD14 primary*	Immune	H3K4me1	3.33
Liver*	Liver	H3K27ac	2.97
Adipose nuclei	Other	H3K9ac	2.71

(d) LDL

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR $<$ 0.05. ** = significant at p $<$ 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Liver (BI)*	Liver	H3K4me1	4.51
Adipose nuclei*	Other	H3K4me1	4.26
Liver*	Liver	H3K27ac	3.61
Adipose nuclei*	Other	H3K9ac	3.34
Adipose nuclei*	Other	H3K4me3	3.08
CD14 primary*	Immune	H3K4me1	2.86
Adipose nuclei*	Other	H3K27ac	2.84
Liver (BI)*	Liver	H3K9ac	2.74
Liver (BI)*	Liver	H3K4me3	2.66

(e) HDL

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR $<$ 0.05. ** = significant at p $<$ 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Liver (BI)*	Liver	H3K4me1	3.99
Liver*	Liver	H3K27ac	3.66
Liver (BI)*	Liver	H3K9ac	3.02
Duodenum Mucosa	GI	H3K4me3	2.71
Liver (UCSD)	Liver	H3K4me3	2.68

(f) Triglycerides

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR $<$ 0.05. ** = significant at p $<$ 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Adipose nuclei*	Other	H3K4me1	4.21
Duodenum Mucosa*	GI	H3K4me1	3.43
Colonic mucosa*	GI	H3K9ac	3.01
Duodenum Mucosa	GI	H3K9ac	2.78
Rectal mucosa	GI	H3K9ac	2.68

(g) Coronary artery disease

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR $<$ 0.05. ** = significant at p $<$ 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Pancreatic islets	Adrenal/Pancreas	H3K4me3	2.87
Pancreatic islets	Adrenal/Pancreas	H3K27ac	2.73
Fetal large intestine	GI	H3K4me1	2.49
Fetal small intestine	GI	H3K4me1	2.31
Adipose nuclei	Other	H3K9ac	2.27

(h) Type 2 Diabetes

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Pancreatic islets*	Adrenal/Pancreas	H3K27ac	3.93
Pancreatic islets*	Adrenal/Pancreas	H3K4me1	3.1
Pancreatic islets	Adrenal/Pancreas	H3K4me3	2.93
Pancreatic islets	Adrenal/Pancreas	H3K4me3	2.25
Fetal small intestine	GI	H3K4me1	2.18

(i) Fasting Glucose

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Fetal brain**	CNS	H3K4me3	18.51
Mid frontal lobe**	CNS	H3K4me3	14.44
Germinal matrix**	CNS	H3K4me3	12.68
Mid frontal lobe**	CNS	H3K9ac	11.27
Angular gyrus**	CNS	H3K4me3	10.89
Inferior temporal lobe**	CNS	H3K4me3	10.77
Cingulate gyrus**	CNS	H3K9ac	10.27
Fetal brain**	CNS	H3K9ac	10.24
Anterior caudate**	CNS	H3K4me3	9.66
Cingulate gyrus**	CNS	H3K4me3	9.34
Pancreatic islets**	Adrenal/Pancreas	H3K4me3	8.65
Anterior caudate**	CNS	H3K9ac	8.5
Angular gyrus**	CNS	H3K9ac	8.33
Mid frontal lobe**	CNS	H3K27ac	8.1
Anterior caudate**	CNS	H3K4me1	7.92
Inferior temporal lobe**	CNS	H3K4me1	7.43
Psoas muscle**	Skeletal Muscle	H3K4me3	7.38
Fetal brain**	CNS	H3K4me1	7.21
Inferior temporal lobe**	CNS	H3K9ac	7.03
Hippocampus middle**	CNS	H3K9ac	6.03
Pancreatic islets**	Adrenal/Pancreas	H3K9ac	5.79
Penis foreskin melanocyte primary**	Other	H3K4me3	5.68
Angular gyrus**	CNS	H3K27ac	5.63
Cingulate gyrus**	CNS	H3K4me1	5.55
Hippocampus middle**	CNS	H3K4me3	5.55
CD34 primary**	Immune	H3K4me3	5.33
Sigmoid colon**	GI	H3K4me3	5.3
Fetal adrenal**	Adrenal/Pancreas	H3K4me3	5.2
Inferior temporal lobe**	CNS	H3K27ac	5.08
Peripheralblood mononuclear primary**	Immune	H3K4me3	5.03
Gastric**	GI	H3K4me3	4.93
Substantia nigra*	CNS	H3K4me3	4.71
Fetal brain*	CNS	H3K4me3	4.58
Hippocampus middle*	CNS	H3K4me1	4.48
Ovary*	Other	H3K4me3	4.19
CD19 primary (UW)*	Immune	H3K4me3	4.15
Small intestine*	GI	H3K4me3	4.07
Lung*	Cardiovascular	H3K4me3	3.93
Fetal stomach*	GI	H3K4me3	3.89
Fetal leg muscle*	Skeletal Muscle	H3K4me3	3.82
Spleen*	Immune	H3K4me3	3.77
Breast fibroblast primary*	Connective/Bone	H3K4me3	3.69
Right ventricle*	Cardiovascular	H3K4me3	3.67
CD4+ CD25- Th primary*	Immune	H3K4me3	3.66
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary*	Immune	H3K4me1	3.66
CD8 naive primary (UCSF-UBC)*	Immune	H3K4me3	3.65
Pancreas*	Adrenal/Pancreas	H3K4me3	3.63
CD4+ CD25- Th primary*	Immune	H3K4me1	3.56
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me1	3.56
Colonic mucosa*	GI	H3K4me3	3.49
Right atrium*	Cardiovascular	H3K4me3	3.48
Fetal trunk muscle*	Skeletal Muscle	H3K4me3	3.47
CD4+ CD25int CD127+ Tmem primary*	Immune	H3K4me3	3.46
Substantia nigra*	CNS	H3K9ac	3.44
Placenta amnion*	Other	H3K4me3	3.38
Breast myoepithelial*	Other	H3K9ac	3.26
CD8 naive primary (BI)*	Immune	H3K4me1	3.24
Substantia nigra*	CNS	H3K4me1	3.18
Cingulate gyrus*	CNS	H3K27ac	3.1
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me3	3.06

(j) Schizophrenia

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Mid frontal lobe*	CNS	H3K27ac	4.42
Penis foreskin keratinocyte primary	Other	H3K9ac	3.05
Fetal brain	CNS	H3K9ac	2.92
Fetal brain	CNS	H3K4me3	2.9
Mid frontal lobe	CNS	H3K4me3	2.78

(k) Bipolar disorder

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Angular gyrus	CNS	H3K9ac	2.61
Mid frontal lobe	CNS	H3K9ac	2.38
Mid frontal lobe	CNS	H3K4me1	2.36
Anterior caudate	CNS	H3K9ac	2.28
Cingulate gyrus	CNS	H3K9ac	2.22

(l) Anorexia

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Angular gyrus**	CNS	H3K4me3	6.63
Fetal brain**	CNS	H3K4me3	6.05
Mid frontal lobe**	CNS	H3K4me3	5.99
Anterior caudate**	CNS	H3K4me3	5.73
Inferior temporal lobe**	CNS	H3K4me3	5.63
CD56 primary**	Immune	H3K4me3	5.32
Germinal matrix**	CNS	H3K4me3	5.29
Mid frontal lobe**	CNS	H3K9ac	5.26
Cingulate gyrus**	CNS	H3K9ac	4.98
Cingulate gyrus**	CNS	H3K4me3	4.94
CD8 naive primary (UCSF-UBC)**	Immune	H3K4me3	4.88
Penis foreskin melanocyte primary*	Other	H3K4me3	4.73
Mid frontal lobe*	CNS	H3K27ac	4.43
Peripheralblood mononuclear primary*	Immune	H3K4me3	4.39
CD34 primary*	Immune	H3K4me3	4.12
Fetal brain*	CNS	H3K9ac	4.03
CD14 primary*	Immune	H3K4me3	4.01
Inferior temporal lobe*	CNS	H3K9ac	3.98
Angular gyrus*	CNS	H3K9ac	3.96
Sigmoid colon*	GI	H3K4me3	3.83
Pancreatic islets*	Adrenal/Pancreas	H3K9ac	3.83
CD4+ CD25int CD127+ Tmem primary*	Immune	H3K4me3	3.72
Anterior caudate*	CNS	H3K9ac	3.65
Hippocampus middle*	CNS	H3K4me3	3.65
CD19 primary (UW)*	Immune	H3K4me3	3.63
Small intestine*	GI	H3K4me3	3.52
CD4+ CD25- Th primary*	Immune	H3K4me3	3.45
Lung*	Cardiovascular	H3K4me3	3.19
CD4+ CD25- CD45R0+ memory primary*	Immune	H3K4me3	3.19
Hippocampus middle*	CNS	H3K9ac	3.17
Liver (UCSD)*	Liver	H3K4me3	3.08
Fetal placenta*	Other	H3K4me3	3.08
Fetal adrenal*	Adrenal/Pancreas	H3K4me3	3.04
Right atrium*	Cardiovascular	H3K4me3	2.99
Pancreatic islets*	Adrenal/Pancreas	H3K4me3	2.96
CD8 naive primary (UCSF-UBC)*	Immune	H3K9ac	2.95
CD3 primary (BI)*	Immune	H3K4me3	2.94
Angular gyrus*	CNS	H3K27ac	2.93
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me3	2.93
Gastric*	GI	H3K4me3	2.92
CD4 naive primary*	Immune	H3K4me3	2.89
CD8 memory primary*	Immune	H3K4me3	2.78
CD3 primary (UW)*	Immune	H3K4me3	2.76
Rectal smooth muscle*	GI	H3K4me3	2.73
Fetal brain*	CNS	H3K4me3	2.67
Esophagus*	GI	H3K4me3	2.66
CD8 naive primary (BI)*	Immune	H3K4me3	2.58
Left Ventricle*	Cardiovascular	H3K4me3	2.56
CD19 primary (BI)*	Immune	H3K4me3	2.56
Fetal thymus*	Immune	H3K4me3	2.52
Breast vHMEC*	Other	H3K4me3	2.51
CD8 primary*	Immune	H3K4me3	2.51
Psoas muscle*	Skeletal Muscle	H3K4me3	2.51
Peripheralblood mononuclear primary*	Immune	H3K9ac	2.5
Ovary*	Other	H3K4me3	2.47
Pancreas*	Adrenal/Pancreas	H3K4me3	2.46
Breast fibroblast primary*	Connective/Bone	H3K4me3	2.45
CD4+ CD25+ CD127- Treg primary*	Immune	H3K4me3	2.36
Placenta amnion*	Other	H3K4me3	2.34
Right ventricle*	Cardiovascular	H3K4me3	2.33

(m) Years of education

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
Inferior temporal lobe*	CNS	H3K4me3	3.21
Cingulate gyrus*	CNS	H3K27ac	3.2
Substantia nigra*	CNS	H3K27ac	3.16
Hippocampus middle*	CNS	H3K27ac	3.13
Breast myoepithelial*	Other	H3K9ac	3.06
Inferior temporal lobe*	CNS	H3K4me1	2.93
Anterior caudate*	CNS	H3K27ac	2.81
Inferior temporal lobe*	CNS	H3K27ac	2.81
Angular gyrus*	CNS	H3K27ac	2.77
Pancreatic islets*	Adrenal/Pancreas	H3K4me1	2.55

(n) Ever smoked

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at p < 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary**	Immune	H3K4me1	6.76
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary**	Immune	H3K4me1	6.11
CD4+ CD25- CD45R0+ memory primary**	Immune	H3K4me1	5.92
CD4 memory primary**	Immune	H3K4me1	5.88
CD4+ CD25+ CD127- Treg primary**	Immune	H3K4me1	5.83
CD25- IL17- Th stim MACS**	Immune	H3K27ac	5.7
Th2**	Immune	H3K27ac	5.5
CD8 memory primary**	Immune	H3K4me1	5.38
CD4 naive primary**	Immune	H3K4me1	5.26
CD4+ CD25- Th primary**	Immune	H3K4me1	5.25
CD19 primary (UW)**	Immune	H3K4me1	5.25
CD4+ CD25int CD127+ Tmem primary**	Immune	H3K4me1	4.88
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me1	4.75
CD3 primary (BI)*	Immune	H3K4me1	4.64
CD3 primary (UW)*	Immune	H3K4me1	4.63
CD25- IL17+ Th17 stim*	Immune	H3K27ac	4.55
CD8 naive primary (UCSF-UBC)*	Immune	H3K4me1	4.49
CD8 naive primary (BI)*	Immune	H3K4me1	4.45
Th0*	Immune	H3K27ac	4.09
CD25+ CD127- Treg*	Immune	H3K27ac	4.09
Th1*	Immune	H3K27ac	3.96
CD19 primary (BI)*	Immune	H3K4me1	3.91
CD56 primary*	Immune	H3K4me1	3.77
Treg primary*	Immune	H3K4me3	3.63
CD3 primary*	Immune	H3K27ac	3.62
CD20*	Immune	H3K27ac	3.45
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary*	Immune	H3K4me3	3.45
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary*	Immune	H3K4me3	3.17
CD4+ CD25+ CD127- Treg primary*	Immune	H3K4me3	3.1
CD4+ CD25int CD127+ Tmem primary*	Immune	H3K4me3	2.76
Peripheralblood mononuclear primary*	Immune	H3K9ac	2.58
CD25int CD127+ Tmem*	Immune	H3K27ac	2.27
CD4+ CD25- CD45R0+ memory primary*	Immune	H3K4me3	2.24
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me3	2.2
CD8 memory primary*	Immune	H3K4me3	2.17
CD19*	Immune	H3K27ac	2.13
CD4 memory primary*	Immune	H3K4me3	2.12
Peripheralblood mononuclear primary*	Immune	H3K4me1	2.12
CD4+ CD25- Th primary*	Immune	H3K4me3	1.98

(o) Rheumatoid arthritis

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at p < 0.05 after correcting for multiple hypotheses.

Cell type	cell-type group	Mark	$-log_{10}(p)$
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary**	Immune	H3K4me1	7.59
Th1**	Immune	H3K27ac	6.54
CD25- IL17+ Th17 stim**	Immune	H3K27ac	6.5
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary**	Immune	H3K4me1	6.24
CD4 memory primary**	Immune	H3K4me1	5.88
Th2**	Immune	H3K27ac	5.87
CD4+ CD25- Th primary**	Immune	H3K4me1	5.59
CD8 memory primary**	Immune	H3K4me1	5.13
CD14 primary**	Immune	H3K4me1	5.03
CD3 primary (UW)**	Immune	H3K4me1	4.96
Th0*	Immune	H3K27ac	4.8
CD56 primary*	Immune	H3K4me1	4.8
CD25- IL17- Th stim MACS*	Immune	H3K27ac	4.72
CD4+ CD25- CD45R0+ memory primary*	Immune	H3K4me1	4.7
CD4 naive primary*	Immune	H3K4me1	4.51
CD4+ CD25int CD127+ Tmem primary*	Immune	H3K4me1	4.44
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me1	4.36
CD8 naive primary (BI)*	Immune	H3K4me1	4.31
CD19 primary (UW)*	Immune	H3K4me1	4.26
CD8 naive primary (UCSF-UBC)*	Immune	H3K4me1	4.2
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary*	Immune	H3K4me3	4.18
CD19 primary (BI)*	Immune	H3K4me1	4.17
CD3 primary (BI)*	Immune	H3K4me1	3.73
CD4+ CD25+ CD127- Treg primary*	Immune	H3K4me1	3.62
CD3 primary*	Immune	H3K27ac	3.25
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary*	Immune	H3K4me3	3.16
CD34 primary*	Immune	H3K4me1	2.87
Peripheralblood mononuclear primary*	Immune	H3K9ac	2.87
CD15 primary*	Immune	H3K4me1	2.85
Spleen*	Immune	H3K4me1	2.7
CD4 primary*	Immune	H3K4me3	2.49
Peripheralblood mononuclear primary*	Immune	H3K4me1	2.46
CD8 primary*	Immune	H3K4me3	2.44
CD14*	Immune	H3K27ac	2.18
CD4 memory primary*	Immune	H3K4me3	2.12
Colonic mucosa*	GI	H3K4me1	2.11
CD19 primary (BI)*	Immune	H3K4me3	2.1
CD4 naive primary*	Immune	H3K4me3	2.09
Mobilized CD34 primary*	Immune	H3K4me1	2.08
CD25int CD127+ Tmem*	Immune	H3K27ac	2.04

(p) Crohn's disease

Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

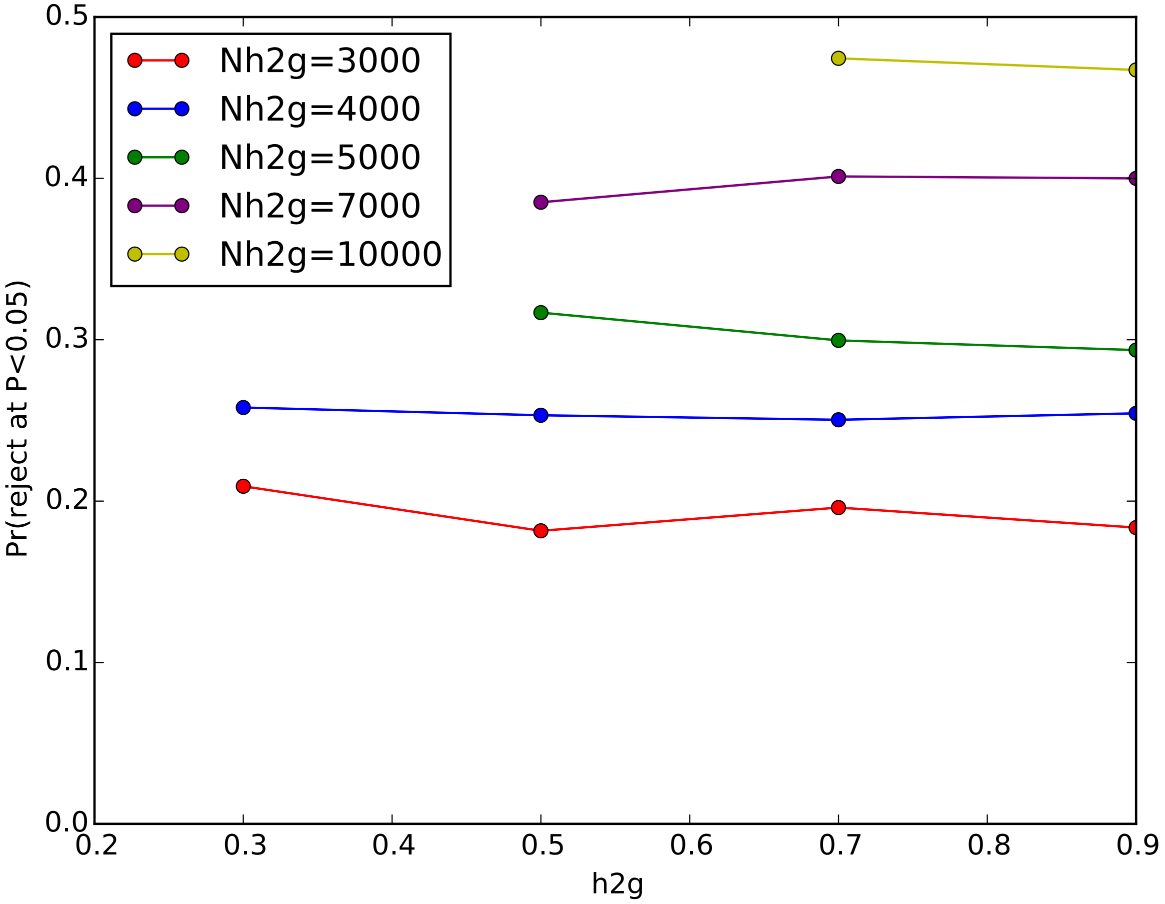
Cell type	cell-type group	Mark	$-log_{10}(p)$
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary**	Immune	H3K4me1	6.37
CD25- IL17+ Th17 stim**	Immune	H3K27ac	5.53
CD4+ CD25- CD45R0+ memory primary**	Immune	H3K4me1	5.48
CD4 memory primary**	Immune	H3K4me1	5.19
CD4+ CD25+ CD127- Treg primary**	Immune	H3K4me1	4.88
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary*	Immune	H3K4me1	4.73
CD3 primary*	Immune	H3K27ac	4.72
Th2*	Immune	H3K27ac	4.5
CD25+ CD127- Treg*	Immune	H3K27ac	4.42
Colonic mucosa*	GI	H3K4me1	4.17
Spleen*	Immune	H3K4me1	4.06
CD4+ CD25- IL17+ PMA Ionomycin stim Th17 primary*	Immune	H3K4me3	4.04
CD4+ CD25- Th primary*	Immune	H3K4me1	4.03
Colonic mucosa*	GI	H3K27ac	4.0
Th1*	Immune	H3K27ac	3.96
CD4 naive primary*	Immune	H3K4me1	3.91
CD4+ CD25int CD127+ Tmem primary*	Immune	H3K4me1	3.87
CD8 memory primary*	Immune	H3K4me1	3.84
Rectal mucosa*	GI	H3K4me1	3.74
CD19 primary (UW)*	Immune	H3K4me1	3.72
Colonic mucosa*	GI	H3K9ac	3.63
Rectal mucosa*	GI	H3K9ac	3.57
CD25- IL17- Th stim MACS*	Immune	H3K27ac	3.54
CD25int CD127+ Tmem*	Immune	H3K27ac	3.45
Th0*	Immune	H3K27ac	3.44
CD8 naive primary (UCSF-UBC)*	Immune	H3K4me1	3.43
CD56 primary*	Immune	H3K4me1	3.21
Rectal mucosa*	GI	H3K27ac	3.16
CD19 primary (BI)*	Immune	H3K4me1	2.95
Treg primary*	Immune	H3K4me3	2.93
CD8 naive primary (BI)*	Immune	H3K4me1	2.91
CD3 primary (UW)*	Immune	H3K4me1	2.83
CD4+ CD25- CD45RA+ naive primary*	Immune	H3K4me1	2.7
CD3 primary (BI)*	Immune	H3K4me1	2.44
Rectal mucosa*	GI	H3K4me3	2.29
CD4+ CD25- IL17- PMA Ionomycin stim MACS Th sprimary*	Immune	H3K4me3	2.24
Duodenum smooth muscle*	GI	H3K27ac	2.17
Duodenum Mucosa*	GI	H3K4me1	2.15
CD34 primary*	Immune	H3K4me1	2.12

(q) Ulcerative colitis

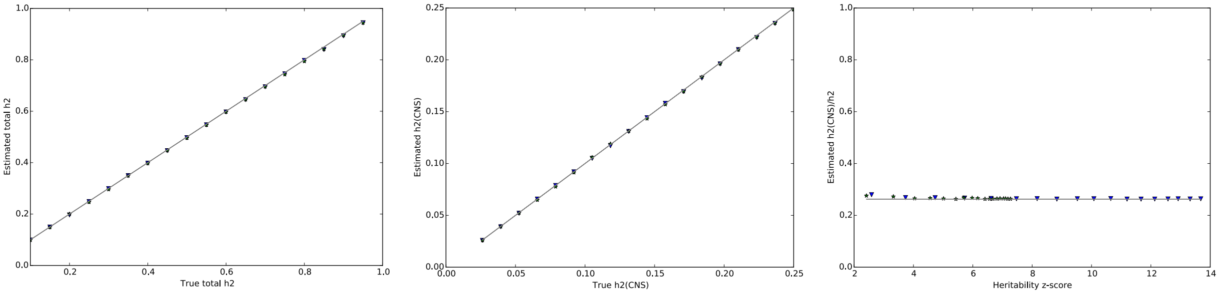
Supplementary Table 7: Enrichment of top cell types for 17 traits. * = significant at FDR < 0.05. ** = significant at $p < 0.05$ after correcting for multiple hypotheses.

Phenotype	Heritability z-score
Type 2 Diabetes	8.12
Ever smoked	8.42
Coronary artery disease	8.71
Ulcerative colitis	8.81
Bipolar disorder	8.81
Triglycerides	9.45
LDL	9.49
Crohn's disease	10.12
Anorexia	10.44
HDL	11.11
Years of education	11.59
BMI	16.79
Age at menarche	16.84
Height	18.89
Schizophrenia	21.29
Rheumatoid arthritis	9.05
Fasting Glucose	7.68

Supplementary Table 8: Heritability z-scores for the 17 traits analyzed in the manuscript



Supplementary Figure 1: N and h_g^2 affect power only through $N \cdot h_g^2$. Sample size is varied to keep $N \cdot h_g^2$ constant as h_g^2 varies. Power stays constant for a given value of $N \cdot h_g^2$.

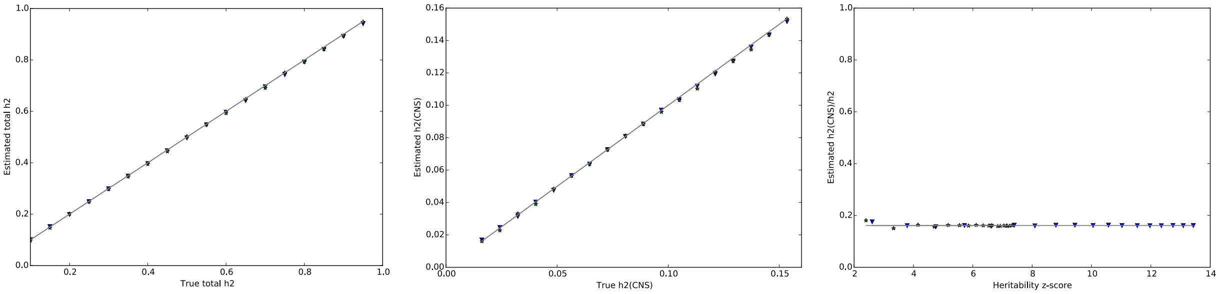


(a) Total h_g^2.

(b) Category-specific h_g^2.

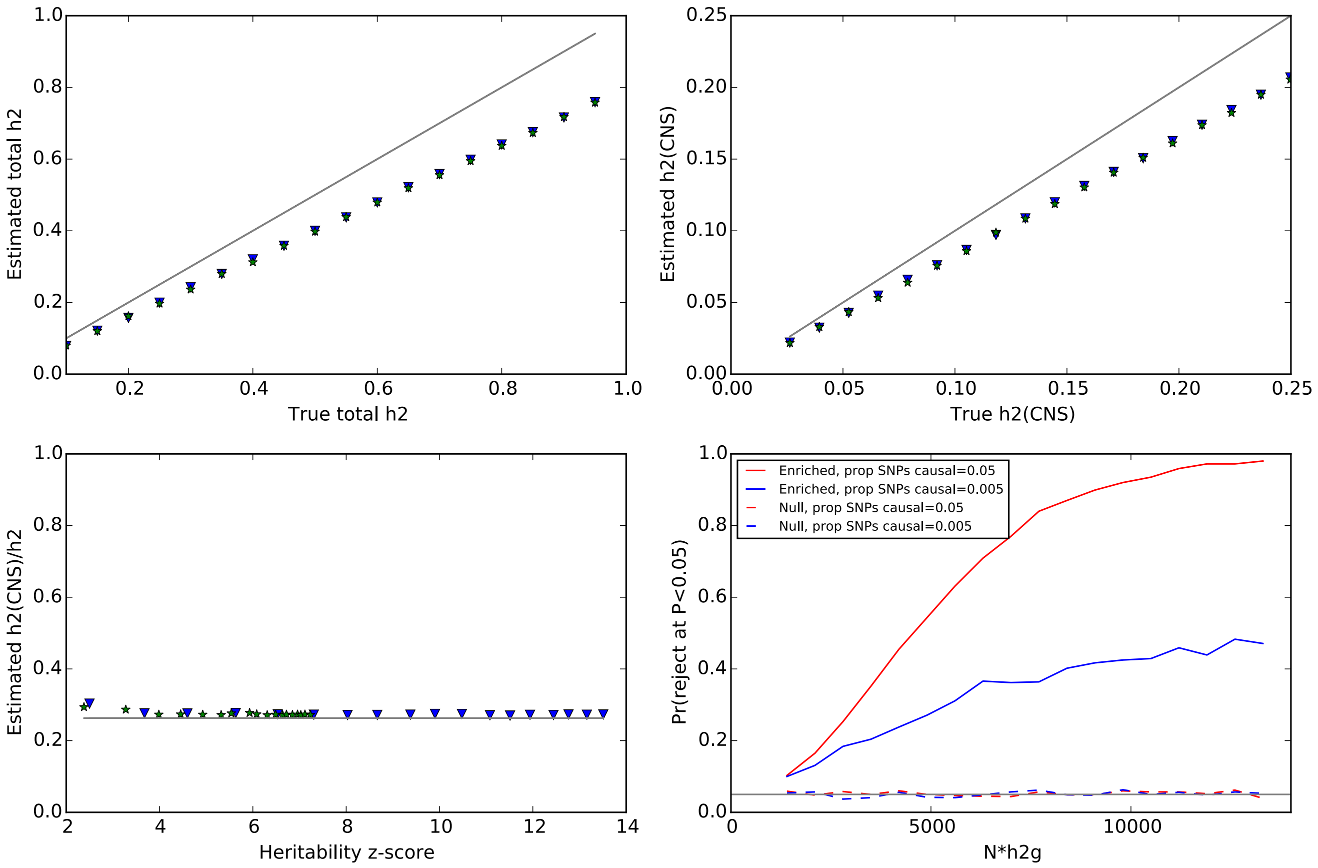
(c) Proportion of h_g^2.

Supplementary Figure 2: Lack of bias in the presence of enrichment. In these simulations, total h_g^2 and proportion of SNPs causal are varied while keeping the proportion of heritability in the tested category constant. The standard error of the mean of each data point is below 0.002.

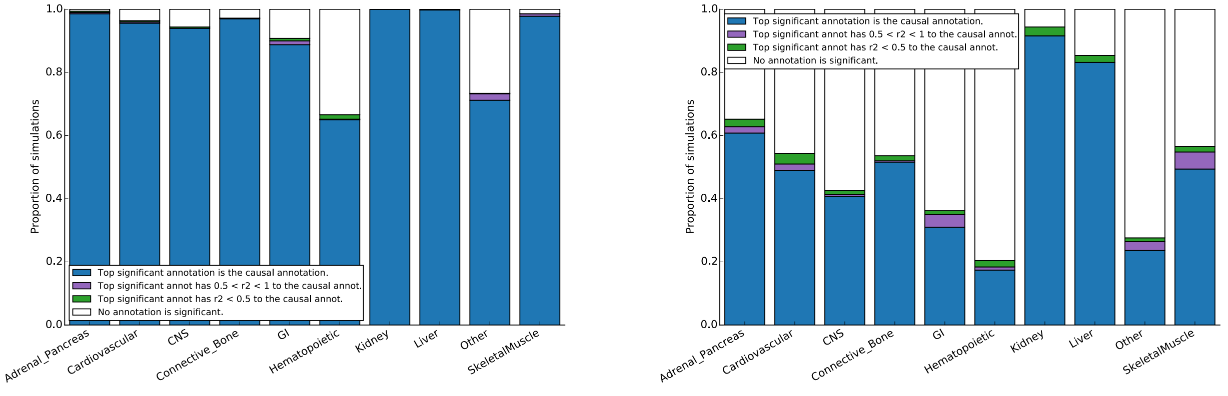


(a) Total h_g^2.
(b) Category-specific h_g^2.
(c) Proportion of h_g^2.

Supplementary Figure 3: Lack of bias in null simulations. In these simulations, total h_g^2 and proportion of SNPs causal are varied. There is no enrichment in these simulations. The standard error of the mean of each data point is below 0.001.



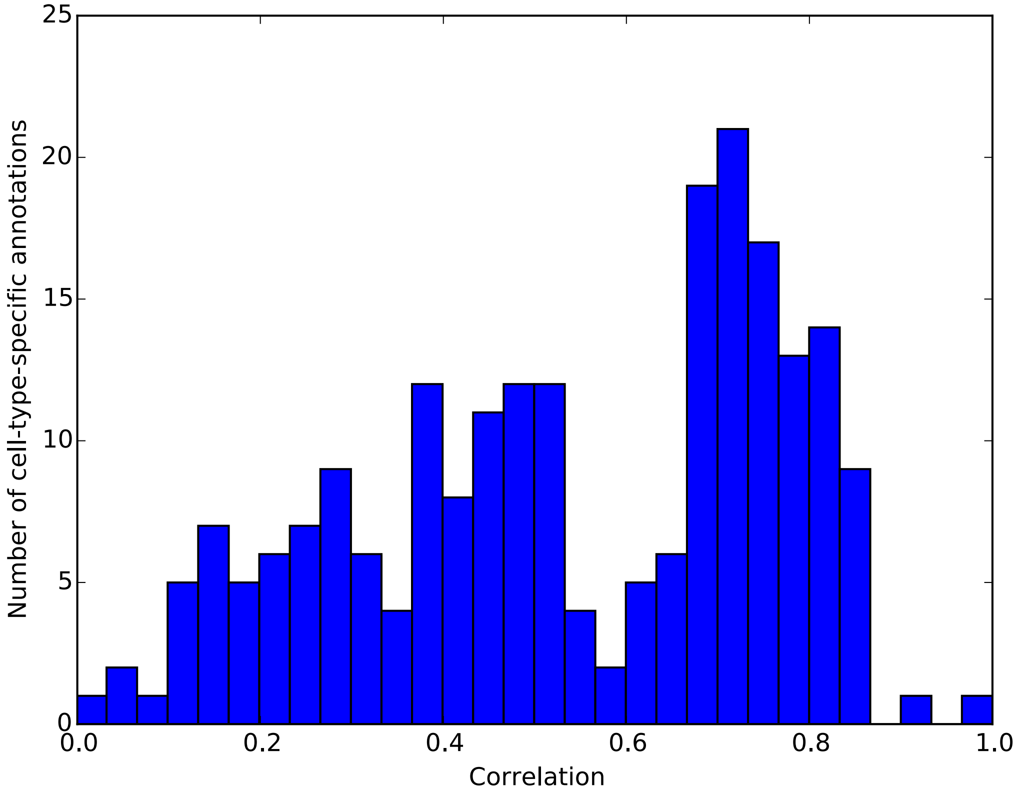
Supplementary Figure 4: Bias and power with an out-of-sample reference panel. In these simulations, WTCCC1 genotypes were used to generate the phenotypes, and stratified LD score regression was run using a 1000G reference panel of European samples, including GBR, FIN, IBS, CEU, and TSI populations.



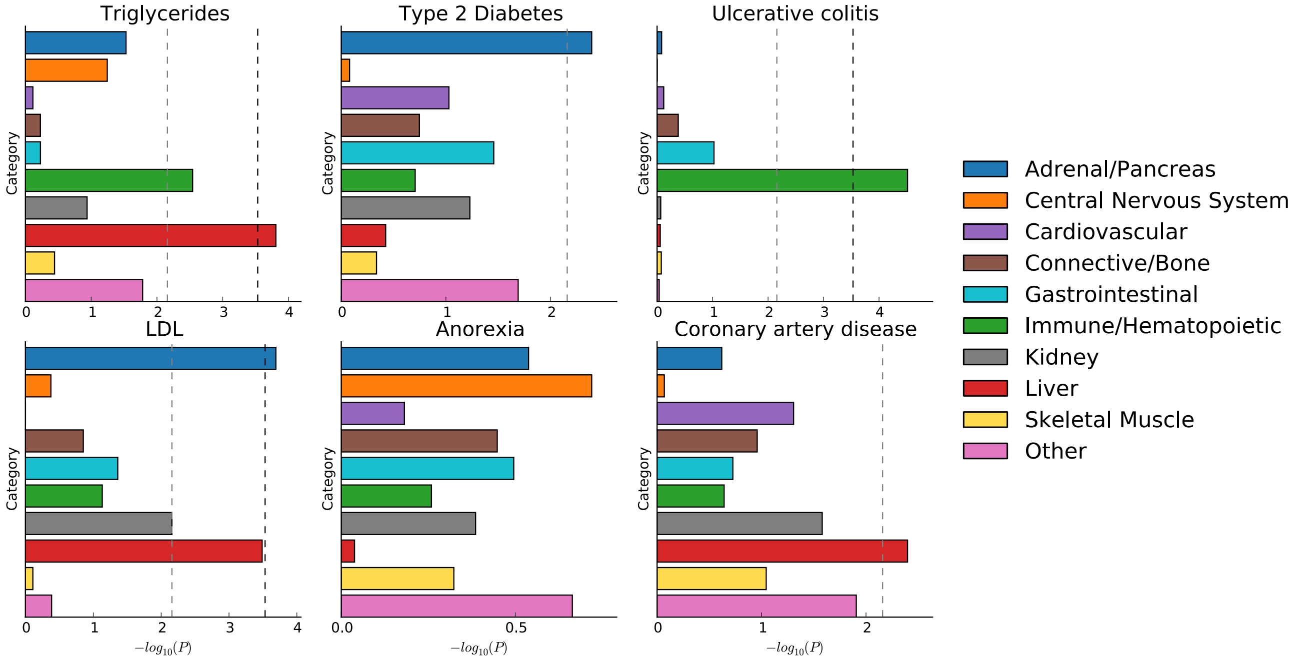
(a) High enrichment.

(b) Low enrichment.

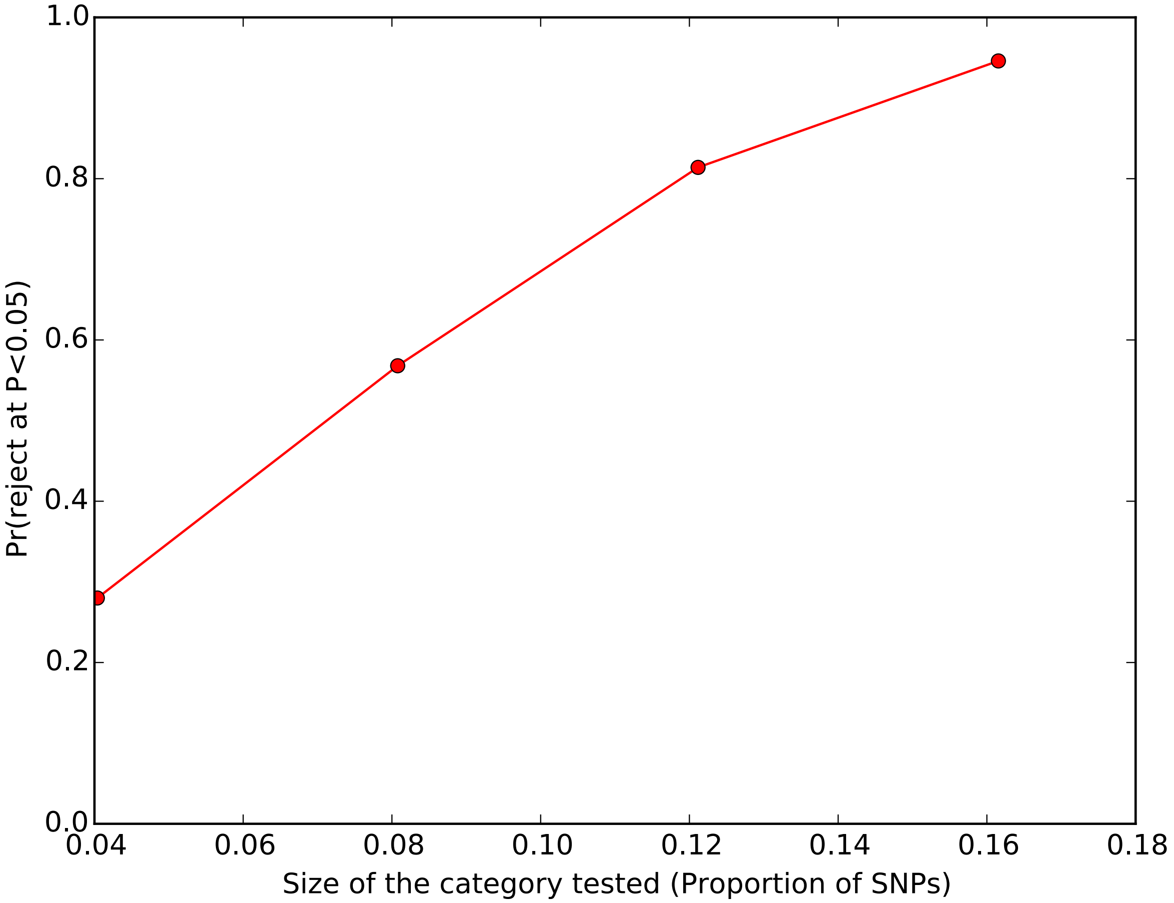
Supplementary Figure 5: Results of Figure 3, broken down by cell-type group.



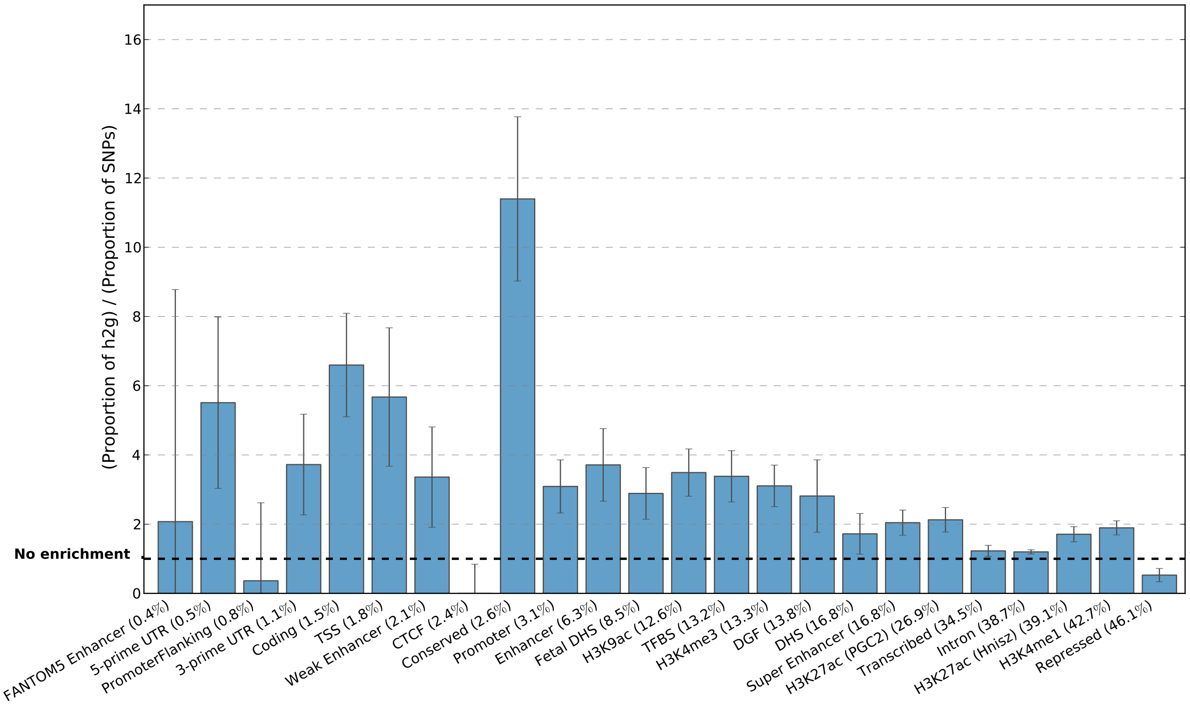
Supplementary Figure 6: Histogram of the correlations of all cell-type-specific annotations with H3K4me3 in Fetal Brain.



Supplementary Figure 7: Enrichment of cell-type groups for traits not included in Figure 6.The black dotted line at $-\log_{10}(P) = 3.5$ is the cutoff for Bonferroni significance. The grey dotted line at $-\log_{10}(P) = 2.1$ is the cutoff for FDR < 0.05.



Supplementary Figure 8: Power as a function of category size. Each point represents a rejection probability over 500 simulations. Baseline enrichment and enrichment in the tested category remain constant as the size of the category changes. All simulations have $h_g^2 = 0.7$, $N = 14000$, $p_{causal} = 0.05$.



Supplementary Figure 9: Enrichment of baseline categories, meta-analyzed over all 17 traits. The standard errors in this analysis are artificially low due to correlated traits such as HDL/LDL/Triglycerides being treated as independent. Results meta-analyzed over nine independent traits are reported in Figure 4.