Extended Data Fig. 9 | GWAS tissue-prioritization. a, Trait-tissue enrichment (centre, heat map) between reported lead single-nucleotide polymorphisms (SNPs) from 226 genome-wide association studies (rows) and accessible active enhancers across 833 biosamples (columns) (FDR <1%). Enriched tissue groups (left) and number of enriched biosamples (right) shown for each trait. Only 83 representative traits labelled, using a bag-of-words approach (full list of traits in Supplementary Fig. 19). Traits coloured by sample with maximal trait-tissue enrichment. b, Contribution of each project to the maximum GWAS trait-tissue enrichment for the 226 traits with significant enrichments.
Extended Data Fig. 10 | GWAS prioritization statistics.

a, Number of traits (y-axis) with significant GWAS trait-tissue enrichments for each combination (column) of projects (rows). b, Increase in the cumulative number of GWAS traits (y-axis) with significant trait-tissue enrichments with increasing numbers of biosamples (x-axis), ordered to maximize the number of novel trait annotations captured with each new biosample. Top 25 samples labelled and coloured by tissue group, with top 6 GWAS traits shown for the first 10 samples. Points coloured by project. All 226 traits are captured after inclusion of 50 samples. c, Increase in the cumulative number of GWAS traits (y-axis) with maximal trait-tissue enrichments with increasing numbers of biosamples (x-axis). All 226 traits are captured after inclusion of 115 samples. d, Comparison of GWAS enrichments found (y-axis, left) and number of lead SNPs in significantly-enriched annotations (y-axis, right) using different methodologies (x-axis) for two FDR cut-offs (shades).
Overlap in enriched GWAS traits between pairs of tissues with maximal enrichment (red x-axis, top) across 232 traits. For each tree node label, the number of GWAS traits (black x-axis, bottom) showing maximum enrichment in that tree node (dark bars, principal tissue) or overlap in enriched GWAS traits between pairs of tissues with maximal enrichment (red x-axis, top) across 232 traits.

Extended Data Fig. 11 | Tissue-tissue GWAS relationships. Principal and partner tissue enrichments. a, For each tree node label (rows), the number of GWAS traits (black x-axis, bottom) showing maximum enrichment in that tree node (dark bars, principal tissue) or any enrichment in that tree node (light bars, partner tissue), and the percentage of tissue-enriched traits for which the tissue shows the maximal enrichment (red x-axis, top) across 232 traits. b, Overlap in enriched GWAS traits between pairs of tissues with maximal enrichment in the trait (principal tissue, rows) and lower enrichment in the same trait (partner tissue, columns), using tree node labels. c, Top traits in significant interactions for selected tissue pairs (liver, endocrine, muscle, heart, adipose, PNS). For each pair of co-enriched tissue groups we reported the top 5 GWAS by their per cent of significant enrichments coming from either group.
Figure S19: All epigenome trait enrichments at FDR of 1%, for 226 traits (rows) and 833 epigenomes (columns)
Figure S20: All module trait enrichments at FDR of 1%, for 93 traits (rows) and 300 modules (columns). Modules are ordered as in Figure 2a.
Figure S21: Overall tissue-level prioritization of 230 traits at FDR of 1%. Heatmap represents trait (rows) vs. tissue matrix and is split for visibility. Traits are diagonalized according to their top tissue enrichment, and values are the trait-normalized and tissue aggregated -log10 p-values.
Figure S22: Trait-trait network (as Figure 3) across 215 traits by similarity of epigenetic enrichments (cosine similarity >= 0.75), laid out using the Fruchterman-Reingold algorithm. Traits (nodes) are colored by contributing groups (pie chart by fraction of -log_{10} p. size by maximal -log_{10} p) and interactions (edges) by the group with maximal dot product of enrichments between two traits. All 215 traits labeled.
Empirical FDR for original and revised EpiMap GWAS enrichment analyses. a, Empirical FDR estimates for three GWAS enrichments analyses (on epigenomes, modules, and tree nodes) for original and revised methodologies. b, Empirical FDR estimates for enhancer sets, binned by number of enhancers in the set for each of the original three analyses. Numbers are the number of original enrichments in each bin. c, Empirical FDR estimates for GWAS, binned by number of SNPs in each GWAS for each of the original three analyses. Numbers are the number of original enrichments in each bin.