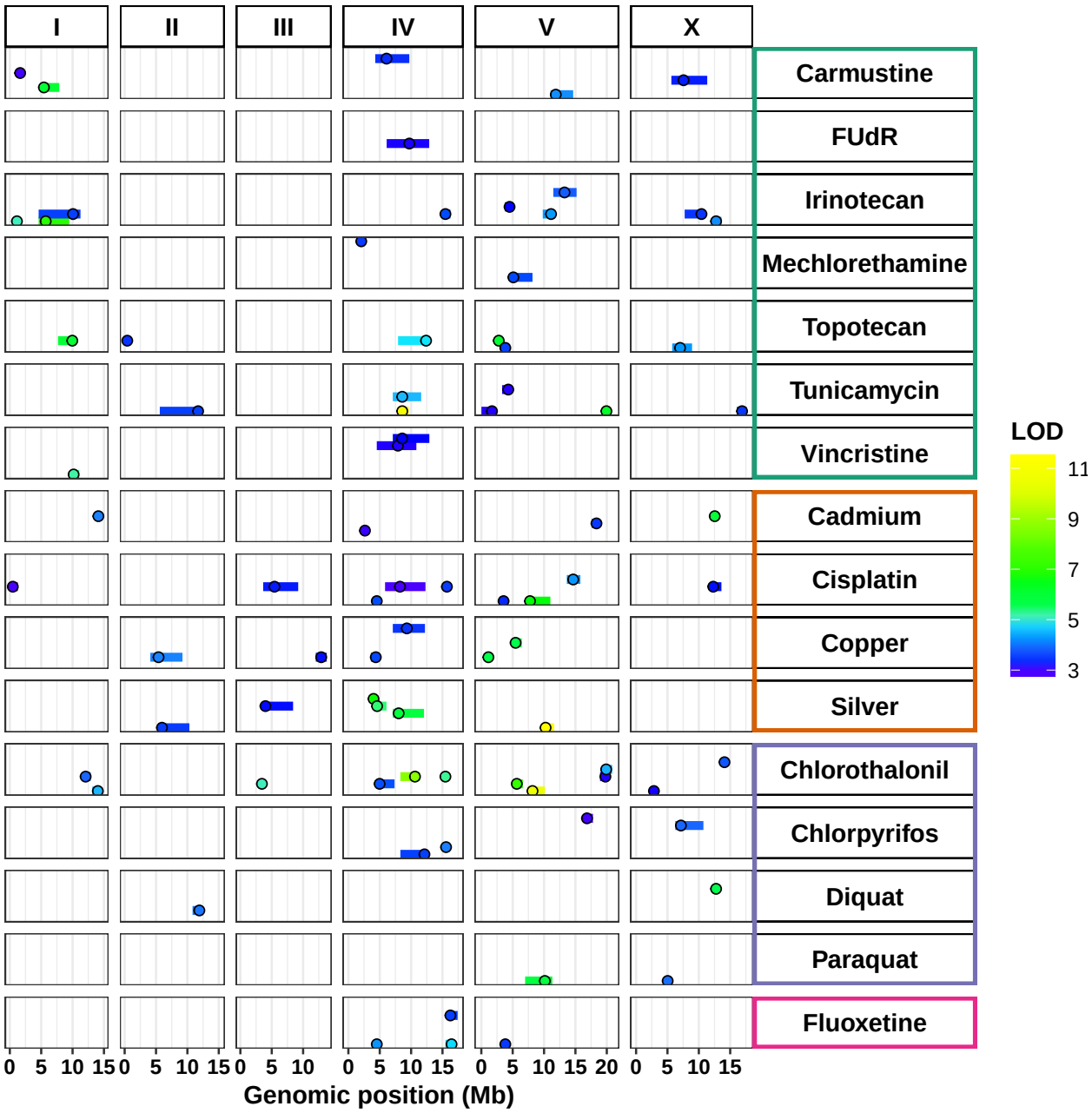

Figure 1 Diverse genetic architectures are implicated in responses to 16 toxins. Linkage mapping results for traits that represent 82 QTL across 16 toxins, comprising chemotherapeutics (teal), heavy metals (orange), pesticides (purple), and neuropharmaceuticals (pink) are plotted. Genomic position (Mb) is shown along the x-axis, split by chromosome, and each trait that represents a QTL is plotted along the y-axis. Each QTL is plotted as a point at the location of the most significant genetic marker and a line indicating the 95% confidence interval. QTL are colored by the logarithm of the odds (LOD) score, increasing in significance from blue to green to yellow.

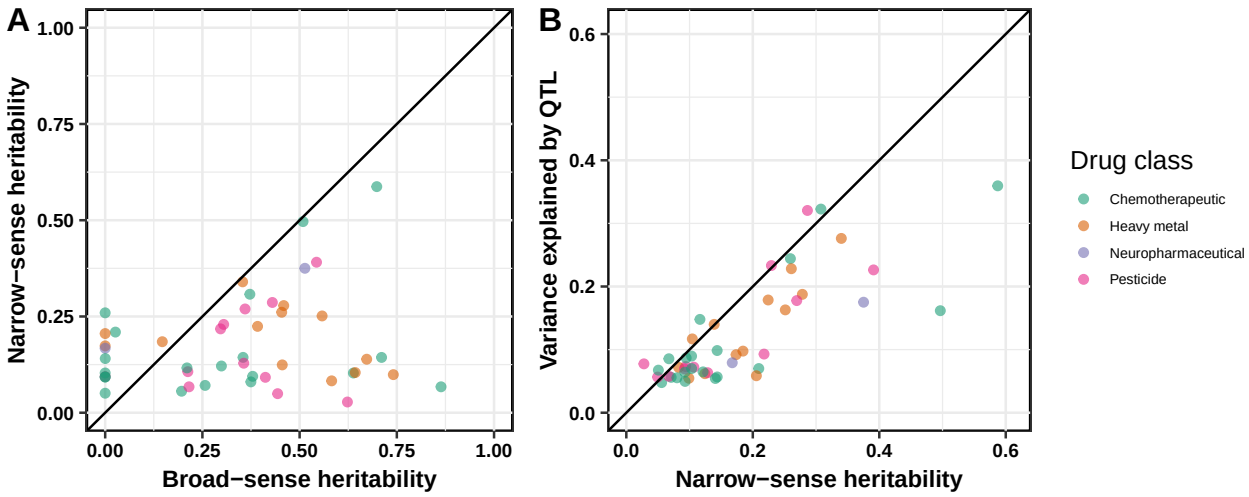

Figure 2 Additive genetic components identified by linkage mapping do not explain all heritable contributions to toxin-response variation. For 47 traits representing the 82 QTL, we compared (**A**) the broad-sense heritability (x-axis) calculated from the dose-response data versus the narrow-sense heritability (y-axis) estimated by linkage mapping and (**B**) the narrow-sense heritability (x-axis) versus the variance explained by all QTL detected by linkage mapping (y-axis). In both plots, each trait is plotted as a point whose color indicates drug class (chemotherapeutic, heavy metal, neuropharmaceutical, or pesticide). The diagonal line represents y = x and is shown as a visual guide.

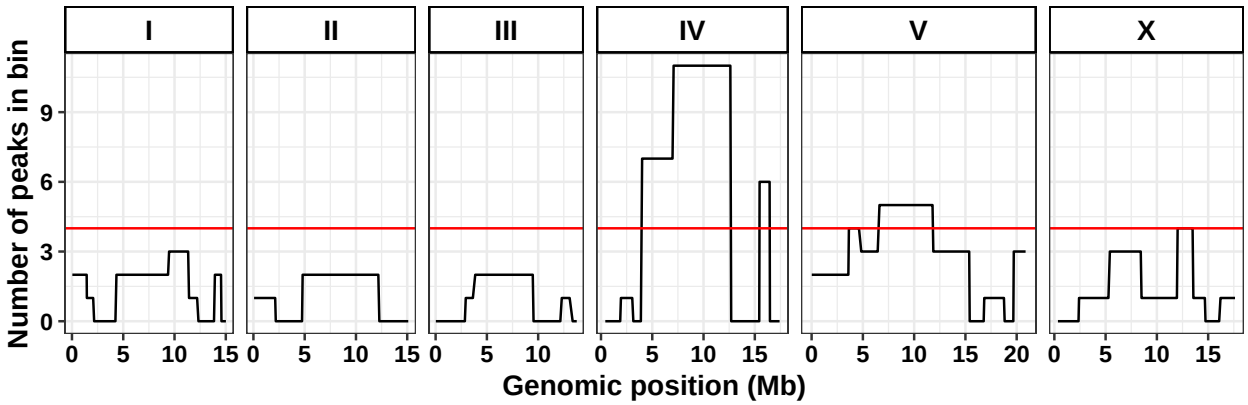

Figure 3 Three QTL hotspots impact condition responses. Each chromosome is divided into equal bins of 26 cM, resulting in a total of 65 bins across the genome. The x-axis shows the genomic position (Mb), and the y-axis shows the number of the QTL that lie within the corresponding bin. The red line indicates the 99th percentile of a Poisson distribution with a mean of1.26 QTL (total QTL/total bins).

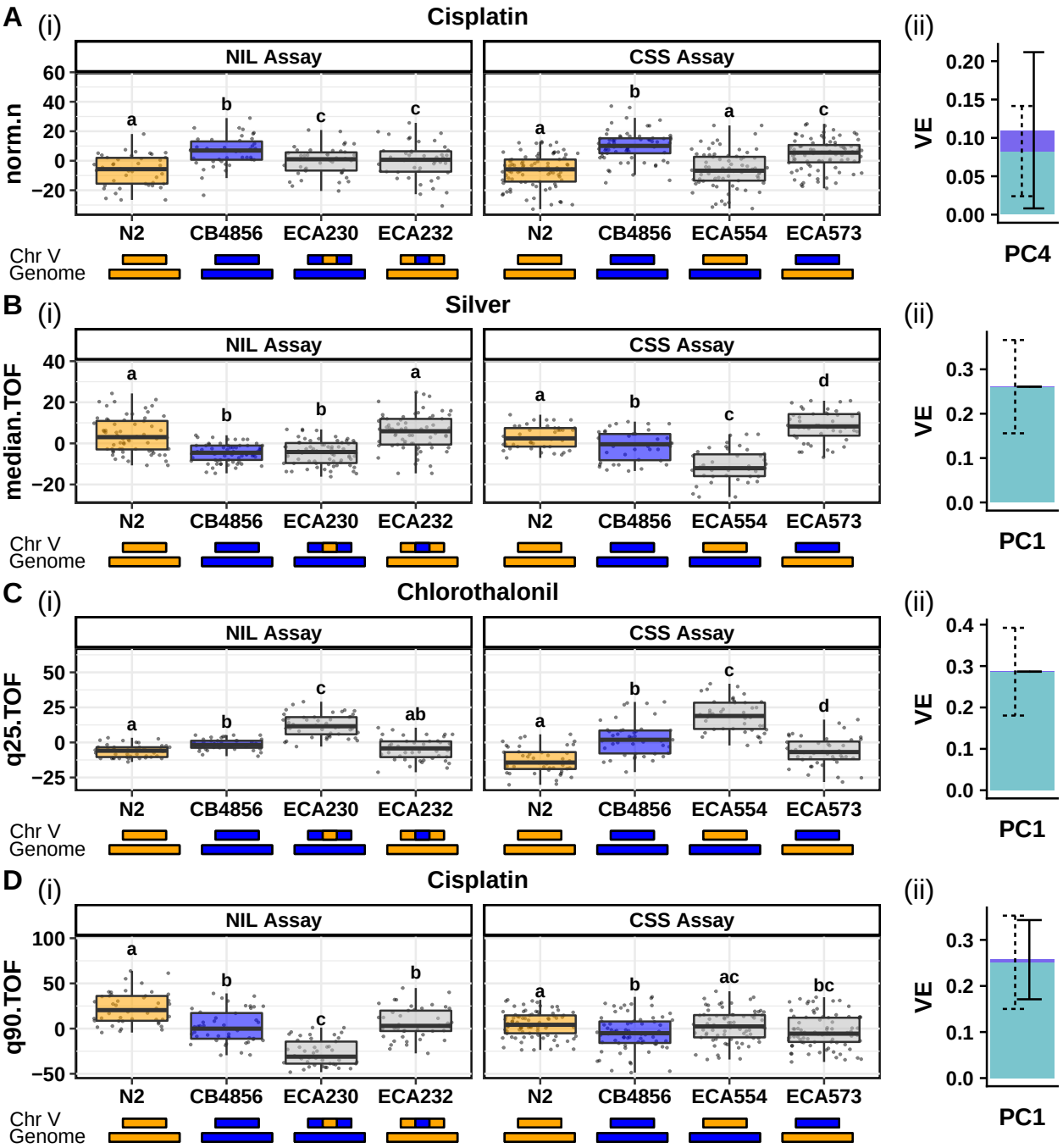

Figure 4 Results from near-isogenic line (NIL) and chromosome-substitution strain (CSS) assays are categorized based on potential variance components implicated in toxin responses. A trait contributing to a mapped principal component for each variance componenet category [(**A**) Recapitulation (cisplatin norm.n, PC1), (**B**) Interchromosomal external bidirectional loci (silver median.TOF, PC1), (**D**) Interchromosomal internal unidirectional loci (chlorothalonil q25.TOF, PC1), and (**E**) Intra-chromosomal unidirectional loci (cisplatin q90.TOF, PC1)] is reported. In each case, we show results from (i) the NIL assay (left) and CSS assay (right) plotted as Tukey box plots. The y-axis indicates residual phenotypic values for the given trait. Different letters (*a-d*) above each Tukey box plot represent significant differences ($p < 0.05$) while the same letter represents non-significant differences between two strains (Tukey HSD). The genotype of each strain on the x-axis is modeled by the colored rectangles beneath the plots (N2 genotypes are orange, CB4856 genotypes are blue). (ii) A stacked bar plot shows the the proportion of phenotypic variation attributable to

additive (light blue with dashed error bars) and interactive (dark blue with solid error bars) genetic factors of the principal component represented by each trait, based on a mixed model.

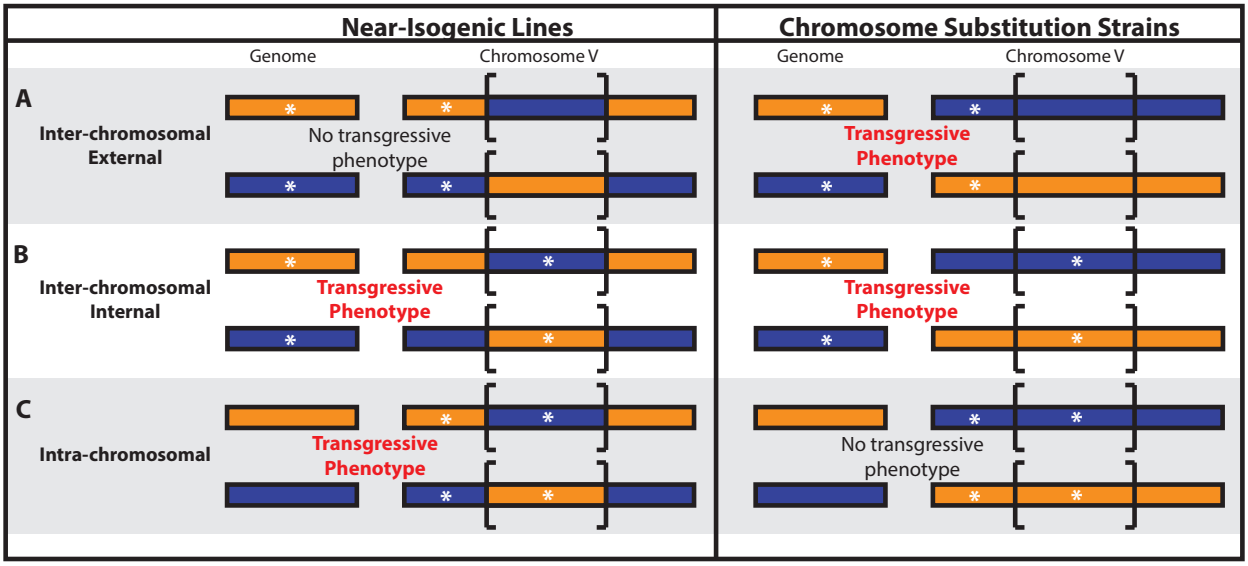

Figure 5 Model of potential additive or interacting loci that could cause hypersensitivity or hyper-resistance in introgressed strains. A model for potential locations of two loci is shown, according to toxin-response phenotypes of near-isogenic lines (NILs) and chromosome-substitution strains (CSSs). The NILs are represented on the left, and the CSSs are represented on the right. The strain genotype is indicated by colored rectangles. N2 is orange, and CB4856 is blue. Brackets indicate the genomic region that is introgressed in the NILs. White asterisks represent a potential location for additive or epistatic loci underlying transgressive phenotypes. Although bidirectional transgressive phenotype models are shown, each model could be bidirectional (both introgressed strains show transgressive phenotypes) or unidirectional (only one introgressed strain shows a transgressive phenotype). Models showing (**A**) external inter-chromosomal effects between a locus outside of the introgressed region in the NILs and a locus on another chromosome, (**B**) internal inter-chromosomal effects between a locus within the introgressed region in the NILs and a locus on another chromosome, and (**C**) intra-chromosomal effects between a locus within and a locus outside of the introgressed region in the NILs are drawn.