Supplementary Information for
Additive genetic effects in interacting species jointly determine the outcome of caterpillar herbivory
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Materials and Methods

Establishing the primary common garden. We first germinated seeds in pots in a greenhouse in April 2018; the greenhouse was maintained at 24°C. Seeds were planted in Sun Gro Propagation mix # 3 (Sun Gro Horticulture, Agawam, MA, USA) after inoculation with Nitragin Gold Alfalfa (Monsanto, Creve Coeur, MO, USA) and scarification with sandpaper. Then, on May 24th 2018, we transplanted seedlings to the Greenville Experimental Farm on a 16×37 meter (m) plot. Plants were laid out in 15 rows of 72 plants each with 0.5 m spacing along rows and 1 m spacing between rows. We randomized plants with respect to source population and maternal family when planting. Plants were watered ~2–3 times per week using a sprinkler system. After the summer, most of the above ground biomass was removed from each plant, including any seed pods (this was done to prevent recruitment of additional plants). The garden was then allowed to overwinter (alfalfa is a perennial) before it was used the following summer (2019) for our experiment. During 2019, we again watered the garden ~2–3 times per week using a sprinkler system.

DNA extraction and sequencing. We isolated DNA from 1064 M. sativa plants from the Greenville Experimental Farm common garden (16 of the initial 1080 plants died before they could be used in the experiment) and 922 L. melissa caterpillars (some caterpillars were too small when they died to be recovered and used for DNA extraction). pupae or adults reared on these plants (DNA was also isolated from an additional 172 M. sativa and 157 L. melissa as part of a complementary smaller common garden experiment that is described below). Medicago sativa DNA was isolated from dried leaf tissue by Ag Biotech (Ag Biotech, Monterey CA, USA). We isolated DNA from whole caterpillars, pupa or the thorax of adult L. melissa butterflies using Qiagen’s DNeasy Blood & Tissue kit (Qiagen Inc. MA, USA) in accordance with the manufacturer’s recommendation.

We then used previously described procedures to create DNA-fragment libraries for our genotyping-by-sequencing approach (1, 2). This approach has proven successful in the past for both M. sativa and L. melissa (2–4). Briefly, we first digested the DNA from each sample with the restriction enzymes EcoRI and MseI. We then ligated adaptor oligonucleotides to the ends of the digested DNA fragments with T4 DNA ligase. The adaptor oligonucleotides included the Illumina adaptors and unique 8–10 base pair (bp) identification sequences or barcodes. Next, we PCR-amplified each fragment library as described in (2). Amplified fragment libraries were then pooled (with sets of 96 samples combined), purified and size-selected. Size selection was accomplished using a BluePippin (Sage Science Inc., Beverly, MA, USA) by Utah State University’s Genomics Core Facility. Fragments between 300 and 450 bps in length were retained for both M. sativa and L. melissa. After purification and size selection, libraries were further pooled in groups of ~192 or ~384 samples for DNA sequencing.

We sequenced the DNA fragment libraries at the University of Texas Genomic Sequencing and Analysis Facility (Austin, TX, USA). Each of three pools of ~384 M. sativa and three pools of ~384 L. melissa were sequenced on one lane on a NovaSeq with S1 100 bp SR reads. A single pool of 184 M. sativa was sequenced on one lane of NovaSeq with SP 100 bp SR reads. After removing PhiX control sequences, this generated ~2.5 billion reads for M. sativa and ~2.5 billion reads for L. melissa.

DNA sequence alignment and variant calling. We first de-multiplexed the M. sativa and L. melissa reads based on our internal barcode sequences; this was done using a custom Perl script. Next, we aligned the M. sativa sequences to the M. sativa genome (5); this was done using the mem algorithm from bwa (version 0.7.17-r1188) (6). For alignment, we considered internal seeds longer than 1.3× the minimum seed length (set to 15 bps) and output alignments with a minimum mapping quality of 30. We then used samtools (version 1.10) to compress, sort and index the alignments (7). Single nucleotide polymorphisms (SNPs) were next identified using GATK (version 4.1) (8). We first used the GATK HaplotypeCaller to compute genotype likelihoods and generate g.vcf files. For this, we set the expected heterozygosity to 0.001 (across all sites), the minimum base quality to 20, and ploidy to four as part of a complementary smaller common garden (used for the diploid L. melissa). We then filtered the initial set of M. sativa SNPs to retain only SNPs with a mean sequence read depth (per individual) >2×, a minimum of 10 reads supporting the non-reference allele, a maximum absolute value for the base-quality rank-sum test of 3, a maximum absolute value for the mapping-quality rank-sum test of 3, a maximum absolute value for the read-position rank-sum test of 2.5, a minimum ratio of variant confidence to non-reference read depth of 2, a minimum mapping quality of 30, and a minimum base quality of 20. SNPs were then called using the call algorithm with a prior heterozygosity (−P) of 0.001 and a minimum posterior probability of a site being variable of 0.99.

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Inference of genotypes and genetic variation. We estimated genotypes using the Bayesian (ad)mixture model implemented in entropy (version 2.0) (2, 11). This program estimates genotypes for diploids or tetraploids while accounting for uncertainty caused by limited coverage and sequencing error, as captured by genotype likelihoods. The model assumes that the two (diploids) or four (tetraploids) allele copies at each SNP locus are drawn from unknown, hypothetical ancestral populations with each individual having a genome with ancestry from some mixture of these hypothetical populations. This allows the relevant allele frequencies for any given individual to be modeled as a mixture of allele frequency distributions. We estimated genotypes for M. sativa and L. melissa assuming two or three ancestral populations, and using the genotype likelihoods from bcftools (L. melissa) or GATK (M. sativa) as input. Estimates were obtained via Markov chain Monte Carlo (MCMC) with three chains, each with 10,000 iterations and a 5000 iteration burn-in. We set the thinning interval to 5. Point estimates of genotypes were obtained as the posterior mean estimate of the number of non-reference alleles, with the posterior summarized across chains and numbers of populations. Thus genotype estimates take on values between 0 and 2 for L. melissa and 0 and 4 for M. sativa, but are not constrained to be integer valued. We then visualized patterns of genetic variation using a principal component analysis (PCA) via the prcomp function in R, with the centered but not scaled genotype estimates as input (i.e., the covariance matrix). We next calculated pairwise linkage disequilibrium (LD) between all physically linked SNPs for M. sativa and L. melissa. This was done in R using the squared genotypic correlation ($r^2$) as a metric of LD. We then summarized LD by computing medians, 95th percentiles, and 99th percentiles for SNPs separated by different distances (distance windows were used for this). Genetic differentiation among experimental M. sativa or L. melissa based on their population of origin was characterized using Nei’s $F_{ST}$ (also known as Nei’s $G_{ST}$) (12, 13). Specifically, we estimated $F_{ST}$ for each pair of plant or insect populations (localities) as $\frac{1}{2} \sum_{p}^{n} (H_{FT} - H_{SF}) \div \frac{1}{2} \sum_{p}^{n} (H_{FT} + H_{SF})$.

Establishing the Gene Miller Life Science Garden. The Gene Miller Life Science Garden, planted on the Utah State University (USU) campus ∼2.5 km from the main garden (41.742°N, 111.811°W), included plants from six of the 11 M. sativa source sites (30 plants per site from six maternal families) and caterpillars from each of the sites used in the main experiment (see Table S1 for site details). These plants were started in a greenhouse on April 18th 2018, with seeds sown in Sun Gro Propagation mix #3 (Sun Gro Horticulture, Agawam, MA, USA) after inoculation with Nitratin Gold Alfalfa (Monsanto, Creve Coeur, MO, USA) and scarification with sandpaper. The greenhouse was maintained at 24°C without overhead lights. The plants were watered ∼3 times per week throughout the summer. Then, in the fall of 2018, we transplanted the 180 plants into the USU common garden. They were arranged in a randomized-block design with six blocks in the ∼6 m × ∼12 m garden.

Plant trait measurements. We measured a series of morphological traits potentially associated with plant vigor or resistance to insects (e.g., putative structural plant defenses)(14–16) for each of the 1080 M. sativa plants in the Greenville Experimental Farm common garden. In May-June 2019, we measured leaf size (length, width and area), leaf shape (length/width), trichome density, dry leaf weight and specific leaf area (SLA) for each plant. Measurements were based on the middle leaflet from the terminal leaf taken from each of two haphazardly chosen sprigs from the center of the plant (taken from opposite sides). We measured the width (at the widest point) and length (along the midvein) of the middle leaflet with calipers (each leaf comprises three leaflets; measurements were taken to the nearest 1 mm). Next, we calculated leaf area (length × width) and shape (length/width) from these measurements. We then counted the number of trichomes in a ∼2.5 mm diameter circle directly adjacent to the midvein under a microscope at 35× magnification. The two leaflets from each plant were then placed in a coin envelope in a bin with desiccant. The dry weight of these leaflets was measured on a Mettler Toledo XPE105 analytical microbalance (Mettler Toledo) to the nearest 0.01 mg. Leaf area and dry weight were used to calculate SLA (SLA is the ratio of leaf area to dry mass and is often correlated with leaf mechanical properties, such as work to tear, shear or punch) (15). The other leaves from the two sprigs collected from each M. sativa plant were placed in coin envelopes in a bin with desiccant to be dried and preserved for chemical analyses. The height of each plant, measured from the top of the soil to the tip of the longest stem, was also determined. Lastly, leaf toughness was measured using a penetrometer. Toughness was quantified as the mean force required to penetrate six leaflets from the midvein (three leaflets from each of two leaves, each from a different branch) (toughness was measured to the nearest 5 g).

In addition to these morphological traits, we quantified the extent to which each plant had been subject to herbivory in the field. This could be indicative both of the palatability of the plant and of the extent to which it might be mounting an induced response to herbivory. Here, we recorded data from two branches on opposite sides of each plant. On each branch, we counted the number of fully open leaves from the fifth node to the terminal end of the branch, along with the number of these leaves with herbivore damage. From this, we computed the proportion of leaves with herbivory.

Sample extraction and phytochemical analysis. Randomized chemical extractions of foliar tissues were carried out as previously described by (17). Briefly, 10.0 mg of ground plant tissue (Qiagen TissueLyser II, 30 Hz, 1 min) were combined with 2.00 mL of 70% aqueous ethanol and briefly vortexed before 15 minutes of sonication. Sample suspensions were then centrifuged at 500 rpm (Genevac EZ-2) for 10 min before filtering through 1 mL 96 well filter plates (glass fiber, 1 μm, Pall, New York, NY) into 1 mL 96 well plates and sealed with a silicon plate mat (Agilent, Santa Clara, CA). Aliquots of 12 samples from each row were combined into pools. All samples (1 μL) were co-injected with a 1 μL air bubble and 1 μL of digitoxin internal standard (ISD; 50 μM in spectral grade MeOH, Fisher Optima). Between every two rows of samples, pools of those two rows were co-injected with ISD for retention time alignment, monitoring instrument response and structural determination. Analytical samples, pools and ISD blanks were injected onto an Agilent 1290 Infinity II UPLC equipped with a dual-channel variable
wavelength detector ($\lambda = 250$ nm) connected to an Agilent 6560 ion-mobility-quadrupole-time-of-flight mass spectrometer equipped with a Jet Stream electrospray ionization dual source with reference mass infusion and tuned in 1700 m/z mode (IM-Q-TOF; drying gas temperature: 300 °C, drying gas flow: 5 L/m; drying gas flow: 8 L/m nebulizer pressure: 50 psig; sheath gas temperature: 275 °C; sheath gas flow: 8 L/m VCap: 3500 V; nozzle voltage: 1000 V; fragmentor: 300 V; octopole: 750 V). All standards, analytical samples and pools were analyzed in TOF mode (1 spectrum per second) and pools were also analyzed in iterative Auto Q-TOF mode (MS: 3 scans per second; MS/MS: 1 scan per second, collision energy: 20, 40 eV, precursor threshold: 10000 counts). Samples were eluted through an Agilent Poroshell 120 column (EC-C18, 1.9 µm, 2.1 × 100 nm) using a linear gradient comprised of solvent A (0.1% aqueous formic acid) and solvent B (99% acetonitrile containing 1% water and 0.1% formic acid) at 0.5 mL/min over 14 minutes as follows: 0 min: 5% B; 4 min: 50% B; 10-12 min: 100% B, ramp to 0.8 mL/min; 12-14 min: 1% B, ramp from 0.6 to 0.5 mL/min. Data were extracted and aligned using Agilent Profinder v1.0 before loading into Agilent Mass Profiler Professional v.15.1. Compounds in less than 10% of samples were excised before exporting peak areas to a csv file. Using the statistical platform R, peak areas were normalized to ISD and dry plant mass before statistical analysis. Tandem mass spectrometry (MS/MS) data were extracted using the find by Auto MS/MS function in Agilent Mass Hunter Qualitative Analysis before exporting to CEF files for further analysis.

**Structural annotations of phytochemicals.** We annotated the 20 phytochemicals most strongly associated with caterpillar performance. Specifically, for each metabolite, we summed the absolute LASSO regression coefficients of association with the nine caterpillar performance polygenic scores, with each coefficient weighted by the heritability of the performance trait based on the plant genetic data, and then selected the 20 compounds with the largest sums for annotation. Three of these compounds were annotated to a high degree of certainty (Table S12) by comparison of their MS/MS spectra to experimental spectra. Compound PC.38.9 was identified as a phosphatidylcholine (PC 16:3/22:6) using Agilent Lipid Annotator v1.0, whereas tricin 7-glucoside and Apigenin 7-[p-coumaroyl-l-(→2)-glucuronyl-l-(→3)]-glucuronyl-(1→2)-glucuronide were identified based on similarity to experimental spectra found in HMDB (18) and to in silico generated MS/MS spectra using CFM-ID (19). Lipids, peptides, N-acyl amines and phosphatidylcholines (PC) were classified based on high-certainty chemical formulae generated by fragmentation trees created in the Sirius 4 platform for determination of structural information (20). These formulae were either further classified by CANOPUS (21) within the Sirius 4 package, or by searching the formulae within the METLIN mass spectrometric database (22). Compounds were classified as peptides if these were the only hits suggested in METLIN. Peptide classifications derived from CANOPUS or METLIN were confirmed by comparing the exact masses of putative peptides to theoretical masses (within 20 ppm) derived for all possible oligopeptides having 2-5 amino acid residues. One diglyceride was classified by chemical formula search in the LIPID MAPS structure database (23), and one PC was classified based on having similar fragmentation (20 eV; m/z = 227.2022 [88%], 255.2319 [88%], 912.7012 [100%]) to another compound classified as a PC (MESA.122; 20 eV; m/z = 227.1999 [95%], 255.2315 [100%], 824.6479 [54%]), despite having different molecular masses. The remaining five compounds were not found during Auto MS/MS due to insufficient signal within the pools, although the precursor ions were observed. In these cases, one PC was classified by searching the LIPID MAPS structure database and four saponins were classified based on METLIN database hits. Of these, one has been previously found in *Medicago spp* (Medicagenic acid 3-O-beta-D-glucoside) (24). Hits for Kudzusaponin SA2, Quilicia acid 3-[rhamnoyl-(1→3)-[galactosyl-(1→2)]-glucuronide], and 28-Glucosyloleanolic acid 3-[rhamnoyl-(1→2)-galactosyl-(1→3)-glucuronide], not previously found in *Medicago* matched masses for glycosyl analogs of the sapogenins soyasapogeninol A, medicagenic acid and gypsogenin (Table S12) found in the PubChem chemical database (25) and have been observed in *Medicago* (26). While these structures cannot be confirmed without MS/MS spectra, we are confident in their classification as saponins.

**LASSO regression models.** We used least absolute shrinkage and selection operator (LASSO) regression to (i) identify the subset of plant traits with polygenic scores that best predicted caterpillar-performance polygenic scores and (ii) estimate the direction and magnitude of these associations (as captured by the regression coefficients). This approach constitutes a form of regularized regression where a subset of regression coefficients are shrunk to zero (27). Thus, in addition to inducing shrinkage on all coefficients, it serves as an approach for variable (feature) selection. We fit a LASSO regression model for the polygenic scores for each caterpillar performance trait with the 1760 plant trait polygenic scores as potential covariates. This was done with the R package glmmnet (version 4.0-2) (28). Ten-fold cross-validation was used to select a value for the penalty parameter $\lambda$. We then estimated the (shrunk) regression coefficients, the coefficient of determination ($r^2$) and cross-validation $r^2$ (squared correlation between observed and predicted values) using the optimal value for $\lambda$. An additional 10-fold cross-validation procedure was used to compute cross-validation $r^2$ with the optimal value for $\lambda$. We then repeated this entire procedure after randomizing the caterpillar-performance polygenic scores for each performance trait (10 randomized data sets per caterpillar performance trait); this was done to gauge null expectations for the degree of variation in performance polygenic scores explained by chance associations with plant-trait polygenic scores.

We repeated the LASSO regression analyses using principal components (PCs) of the 1760 plant trait polygenic scores as covariates. Our goal here was to determine whether independent (orthogonal) axes of the plant genetic contributions to plant traits were associated with polygenic scores for each caterpillar performance trait. PCA was conducted on standardized polygenic scores (i.e., centered and scaled) in R using the prcomp function. 1064 PCs with non-zero eigenvalues were identified (this is equal to the sample size). We then fit LASSO models with these new covariates, which were also centered and scaled, as described in the preceding paragraph.

We next asked whether plant-trait polygenic scores could explain and predict caterpillar performance at the phenotypic level (i.e., not just the polygenic scores). To do this, we fit analogous LASSO regression models to the observed performance trait.
data, or more specifically to the residuals from the observed data after removing the effects of hatch date and location in the common garden. Here too we analyzed randomized response variables as well to generate null expectations (100 randomized data sets for each performance trait).

Finally, we fit an additional set of LASSO regression models to evaluate the extent to which plant-genetic effects, as captured by the plant-trait polygenic scores, interacted with caterpillar genetics to affect performance. For this analysis, we summarized \textit{L. melissa} caterpillar genetics using a PCA of the centered genotype matrix for the reared caterpillars. We used the first four PCs in the LASSO analysis; this allowed us to test for interactions without including a prohibitively large number covariates in the analysis. We specifically fit models for caterpillar-performance polygenic scores (as inferred from plant genetics) as a function of caterpillar genotype (PCs 1-4), plant-trait polygenic scores (1760 traits), and interactions between each plant-trait polygenic score and each of the four caterpillar genotype PCs. This was done with \textit{glmm} (version 4.0.2) (28) as described for the models without interactions.

**Complementary USU greenhouse experiment.** An additional rearing experiment was conducted to (i) replicate the general effect of \textit{M. sativa} genotype on caterpillar performance and (ii) determine whether different plant genotypes had consistent effects of caterpillar performance across different butterfly populations and species. Thus, this provides an additional, coarse grain, test of additivity versus epistasis with respect to genetic differences among butterfly populations (which might be modest) and among deeply divergent species. In this experiment, we did not analyze genotype directly, but instead used \textit{M. sativa} source population as a proxy for genotype (we reduced other environmental sources of phenotypic variation among populations by growing the plants in a greenhouse, or in a common garden as was the case for the second experiment described further below). Here, 1001 \textit{M. sativa} plants from six source populations (ALP, APLL, AWFS, BST, VUH, and VIC) were grown from seed in a greenhouse at USU (Table S14). The plants were planted in the greenhouse on April 18th 2018, with seeds sown in Sun Gro Propagation mix # 3 (Sun Gro Horticulture, Agawam, MA, USA) after inoculation with Nitragin Gold Alfalfa (Monsanto, Creve Coeur, MO, USA) and scarification with sandpaper. The greenhouse was maintained at 24°C without overhead lights. The plants were watered ~three times per week throughout the summer.

We reared at total of 672 caterpillars from four \textit{L. melissa} (Lycaenidae) populations (6-13 females per population; see Table S14), 133 \textit{Colias eurytheme} (Pieridae) caterpillars and 196 \textit{Vanessa cardui} (Nymphalidae) caterpillars on leaf tissue from the greenhouse-grown plants. \textit{Lycaenides melissa} caterpillars were obtained from wild-caught gravid butterflies as described above (collections were made between June 4th and 20th 2018). \textit{Colias eurytheme} is a legume specialist and caterpillars from this species were obtained by collecting gravid females from our \textit{M. sativa} common garden at the Greenville Experimental Farm in Logan, UT (eggs were collected from 20 females on June 16th 2018). \textit{Vanessa cardui} is a generalist butterfly that rarely feeds on alfalfa. We obtained caterpillars for this species by ordering eggs from Carolina Biological Supply Company (item number 144078, ordered five units of ~30-35 eggs May 22nd 2018) (Burlington, NC, USA).

Caterpillars were kept in incubators and fed plant material from the greenhouse-grown \textit{M. sativa} in the same manner as for the common garden at the Greenville Experimental Farm. The only exception was that we ensured each caterpillar consumed leaves from a single source population (our proxy for genotype for this experiment) rather than a single individual. The specific plants used within each population were rotated haphazardly. As our metrics of caterpillar performance, we measured caterpillar weight at 8 and 14 days of development using a Mettler Toledo XPE105 analytical microbalance (Mettler Toledo). Survival to 8 days, 14 days, pupation and eclosion was also noted.

We then estimated the proportion of the variance in 8-day weight and 14-day weight partitioned among plant and caterpillar population by fitting linear mixed-effect models with restricted maximum likelihood. This was done using the \textit{lmer} function from the \textit{R} package \textit{lme4} (version 1.1.23) (\textit{R} version 4.0.2) (29). We analyzed the data from the three butterfly species separately. Plant source population was included as a random effect for each analysis. Caterpillar population was included as a second random effect for \textit{L. melissa} as the caterpillars came from four source populations. Caterpillar hatch data was included in the models for \textit{L. melissa} and \textit{C. eurytheme}, but not \textit{V. cardui} as hatch occurred mostly on a single day. We evaluated the null hypothesis that the variance associated with each random effect was zero using an exact restricted likelihood ratio test (30, 31). This was done with the function \textit{exactRLRT} from the \textit{R} package \textit{RLRsim} (version 3.1.6) with the null distribution generated from 10,000 simulations (32).

To complement the mapping results above and provide an additional test of genetic variation in \textit{M. sativa} for the morphological traits, we also measured plant height, leaf length, leaf width, leaf area, leaf shape, leaf weight, specific leaf area, leaf toughness and trichome density in the 2018 greenhouse experiment. Measurements were taken as described for the main garden during May 2018. We then estimated the proportion of trait variance attributed to plant population and family using linear mixed-effect models with restricted maximum likelihood. This was done using the \textit{lmer} function from the \textit{R} package \textit{lme4} (version 1.1.23) (\textit{R} version 4.0.2) (29). We tested the null hypothesis that the variance associated with each random effect (population or family) was zero using an exact restricted likelihood ratio test (30, 31). This was done with the function \textit{exactRLRT} from the \textit{R} package \textit{RLRsim} (version 3.1.6) with the null distribution generated from 10,000 simulations (32).

**Complementary Nevada common garden rearing experiment.** Three species of caterpillars were reared on alfalfa from an experimental garden at the University of Nevada, Reno (UNR Main Station Farm; Fig. S1), previously described in (17). Fifty-five individual plants were picked at random from the common garden and harvested throughout the summer of 2018 to support the growth of individually-reared caterpillars that were randomly assigned to specific plants (i.e., each caterpillar was fed the foliage from only one plant). One plant died during the summer, thus 54 plants were ultimately involved in analyses. Cuttings from plants were collected weekly and stored in a refrigerator before being fed to caterpillars in petri dishes.
(with leaves replenished every other day) in a growth chamber at 25°C and a 12-hour light, 12-hour dark cycle. On day 10 of development, caterpillars were weighed to the nearest 0.01 mg on a Mettler Toledo XP26 microbalance as a measure of developmental performance.

The three caterpillar species used in experiments were *V. cardui*, *L. melissa*, and *C. eurytheme*. The first species (*V. cardui*) was ordered as eggs from Carolina Biological Supply Company; eggs of the second species (*L. melissa*) were obtained by caging wild-collected females from a location near Reno, Nevada; similarly, eggs of the third species came from females collected at an agricultural field in Northern California (39.1221°N, 121.9686°W). From each species, 10 caterpillars were assigned to each of the experimental plants (i.e., 550 caterpillars per species). For logistical reasons, we staggered the rearing with *V. cardui* starting on 29 June, *L. melissa* on 13 July, and *C. eurytheme* on 25 July, 2018.

For the results reported here, we calculated median weight per species per plant, and then used Pearson correlations between species (among individual plants) to ask if plants that support higher weight gain for one species of caterpillar support higher weight gain for other species.

Table S1. List of source sites for the *M. sativa* Greenville Experimental Farm common garden or for *L. melissa* caterpillars for the rearing experiment. Site abbreviations and full site names are given, along with the number of families sourced for *L. melissa* and *M. sativa* from each site (the average number of individuals per family is given in parentheses). NA denotes sites from which *L. melissa* and *M. sativa* were not sampled.

| Site | Site name         | Latitude (°N) | Longitude (°W) | *L. melissa* N | *M. sativa* N |
|------|-------------------|---------------|----------------|----------------|---------------|
| AFAL | Fallon, NV        | 39.49         | 118.59         | NA             | 20 (5.2)      |
| ALP  | Alpine, WY        | 43.17         | 111.01         | NA             | 21 (5.1)      |
| APLL | Pole Line Road, CA| 38.59         | 121.73         | NA             | 16 (4.6)      |
| AWFS | Patagonia, NV     | 39.51         | 119.90         | NA             | 21 (4.4)      |
| BST  | Bonneville Shoreline Trail, UT | 41.73 | 111.79 | NA | 18 (4.6) |
| CKV  | Cokeville, WY     | 42.00         | 110.94         | 16 (12.4)      | 21 (4.9)      |
| FRM  | Mainstation Farm, NV | 39.51 | 119.72 | NA | 20 (5.0) |
| FRP  | Frary Peak, UT    | 40.98         | 112.22         | 5 (12.2)       | NA            |
| HBR  | Heber, NV         | 40.53         | 111.48         | NA             | 21 (4.8)      |
| HLK  | Honey Lake, CA    | 40.24         | 120.31         | 12 (16.5)      | NA            |
| LK   | Likely, CA        | 41.23         | 120.50         | NA             | 20 (4.7)      |
| SIN  | Sinclair, WY      | 41.86         | 107.09         | 20 (16.2)      | NA            |
| VIC  | Victor, ID        | 43.66         | 111.11         | 13 (15.7)      | 21 (5.1)      |
| VUH  | Verdi, NV         | 39.51         | 112.00         | 16 (4.9)       | 21 (4.8)      |

Table S2. Bayesian estimates of the proportion of genetic variation in caterpillar performance traits explained by *M. sativa* genetics, *L. melissa* genetics, or both combined as inferred from fitting Bayesian sparse linear mixed models with *gemma*. Traits shown are W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Posterior medians (med) and lower (lb) and upper bounds (ub) of Bayesian equal-tail probability intervals are given.

| Trait | *M. sativa* | L. melissa | Combined |
|-------|-------------|------------|----------|
|       | med | lb | ub | med | lb | ub | med | lb | ub |
| W8d   | 0.11 | 0.03 | 0.23 | 0.29 | 0.20 | 0.38 | 0.32 | 0.17 | 0.48 |
| W14d  | 0.36 | 0.23 | 0.50 | 0.12 | 0.04 | 0.23 | 0.49 | 0.34 | 0.64 |
| WPup  | 0.16 | 0.02 | 0.42 | 0.05 | 0.00 | 0.19 | 0.23 | 0.03 | 0.53 |
| S8d   | 0.02 | 0.00 | 0.09 | 0.21 | 0.14 | 0.27 | 0.17 | 0.10 | 0.25 |
| S14d  | 0.03 | 0.00 | 0.10 | 0.19 | 0.13 | 0.25 | 0.16 | 0.11 | 0.22 |
| SPup  | 0.21 | 0.12 | 0.31 | 0.05 | 0.01 | 0.13 | 0.26 | 0.14 | 0.38 |
| SAdu  | 0.13 | 0.04 | 0.24 | 0.11 | 0.04 | 0.21 | 0.17 | 0.07 | 0.28 |
| Stot  | 0.04 | 0.00 | 0.11 | 0.20 | 0.13 | 0.26 | 0.17 | 0.10 | 0.26 |
| Stime | 0.10 | 0.02 | 0.20 | 0.14 | 0.08 | 0.20 | 0.18 | 0.10 | 0.30 |
Table S3. Bayesian estimates of the proportion of genetic variation in caterpillar performance traits explained by *M. sativa* genetics, *L. melissa* genetics, or both combined that is explained by measurable SNP-performance associations as inferred from fitting Bayesian sparse linear mixed models with *gemma*. Traits shown are W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Posterior medians (med) and lower (lb) and upper bounds (ub) of Bayesian equal-tail probability intervals are given.

| Trait | med | lb  | ub  |
|-------|-----|-----|-----|
| M. sativa |     |     |     |
| W8d   | 0.31| 0.00| 0.91|
| W14d  | 0.30| 0.00| 0.87|
| WPup  | 0.26| 0.00| 0.89|
| S8d   | 0.35| 0.00| 0.93|
| S14d  | 0.34| 0.00| 0.93|
| SPup  | 0.24| 0.02| 0.63|
| SAdu  | 0.17| 0.00| 0.78|
| Stot  | 0.44| 0.00| 0.94|
| Stime | 0.18| 0.00| 0.82|
| L. melissa |     |     |     |
| W8d   | 0.84| 0.61| 0.98|
| W14d  | 0.28| 0.00| 0.85|
| WPup  | 0.34| 0.00| 0.93|
| S8d   | 0.97| 0.89| 1.00|
| S14d  | 0.95| 0.83| 1.00|
| SPup  | 0.30| 0.00| 0.90|
| SAdu  | 0.72| 0.16| 0.98|
| Stot  | 0.88| 0.68| 0.99|
| Stime | 0.68| 0.41| 0.94|
| Combined |     |     |     |
| W8d   | 0.35| 0.09| 0.78|
| W14d  | 0.28| 0.01| 0.73|
| WPup  | 0.25| 0.00| 0.88|
| S8d   | 0.90| 0.68| 0.99|
| S14d  | 0.89| 0.66| 0.99|
| SPup  | 0.43| 0.11| 0.86|
| SAdu  | 0.43| 0.11| 0.86|
| Stot  | 0.81| 0.54| 0.98|
| Stime | 0.46| 0.25| 0.84|
Table S4. Bayesian estimates of the number of genetic variants with measurable associations (effects) on caterpillar performance in *M. sativa* genetics, *L. melissa* genetics, or both combined as inferred from fitting Bayesian sparse linear mixed models with *gemma*. Traits shown are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Posterior medians (med) and lower (lb) and upper (ub) bounds of Bayesian equal-tail probability intervals are given.

| Trait | M. sativa | L. melissa | Combined |
|-------|-----------|------------|----------|
|       | med | lb | ub | med | lb | ub | med | lb | ub |
| W8d   | 23  | 0  | 211| 13  | 7  | 23 | 7   | 1  | 206|
| W14d  | 100 | 1  | 286| 8   | 0  | 161| 51  | 1  | 263|
| WPup  | 12  | 0  | 189| 10  | 0  | 178| 15  | 0  | 160|
| S8d   | 6   | 0  | 240| 10  | 5  | 16 | 5   | 2  | 10 |
| S14d  | 5   | 0  | 128| 6   | 3  | 12 | 3   | 2  | 5  |
| SPup  | 8   | 1  | 75 | 14  | 0  | 247| 24  | 0  | 233|
| SAdu  | 12  | 0  | 237| 7   | 2  | 31 | 5   | 1  | 70 |
| Stot  | 4   | 0  | 55 | 5   | 3  | 11 | 3   | 2  | 7  |
| Stime | 21  | 0  | 246| 1   | 1  | 4  | 1   | 1  | 2  |
Table S5. Summary of traits and genes associated with SNPs with posterior inclusion probabilities (PIPs) of > 0.5 for at least one caterpillar performance trait. The chromosome and position of each SNP is given, along with the trait(s) for which it has a PIP > 0.5. Traits shown are W8d = 8-day weight, S8d = 8-day survival, S14d = 14-day survival, Stot = total survival time, and Stime = (truncated) survival time. Then, for each SNP, the nearest annotated gene (if < 50 kbps away) is given, along with the distance to the boundary of the gene. No chromosome is given for the last SNP, but instead the scaffold number if reported (1260); this scaffold most likely corresponds to the genome of the bacterial endosymbiont Wolbachia.

| Chromosome | Position (bp) | Traits          | Gene ID                                      | Distance (kbp) |
|------------|---------------|-----------------|----------------------------------------------|----------------|
| 1          | 18,994,990    | S8d             | NA                                           | NA             |
| 1          | 26,801,442    | S8d, S14d, Stot | NA                                           | NA             |
| 2          | 5,400,668     | W8d             | Vacuolar protein sorting-associated protein 13| 4              |
| 2          | 8,585,087     | Sadu            | V-type proton ATPase 116 kDa subunit a        | 13             |
| 5          | 14,087,514    | Stot            | NA                                           | NA             |
| 8          | 10,131,457    | W8d             | Nesprin-1/MSP-300                            | 2              |
| 8          | 14,984,485    | W8d             | Lipase member H                              | <1             |
| 8          | 15,768,108    | W8d             | Juvenile hormone acid O-methyltransferase    | 9              |
| 16         | 10,535,866    | W8d             | NA                                           | NA             |
| NA-1260    | 1,620,413     | Stime           | Ankyrin                                      | 8              |
Table S6. Summary of *M. sativa* genes within 30 kbps of the single SNP (chromosome 1, position 12,930,966) strongly associated with caterpillar performance (posterior inclusion probability for survival to pupation = 0.65). Gene locations (boundaries) were taken from the *M. sativa* genome annotation (5), and gene identifications were then obtained by submitting the gene sequence to NCBI BLAST data base via the megablast algorithm (accessed December 13th, 2021).

| Gene ID                                      | Location (bps)      | Distance to SNP (bps) |
|----------------------------------------------|---------------------|-----------------------|
| Dentin sialophosphoprotein                   | 12,898,211–12,909,201 | 21,765                |
| Unknown gene                                 | 12,913,180–12,915,634 | 15,332                |
| Photosystem I reaction center subunit psaK   | 12,917,170–12,918,098 | 12,868                |
| DEAD-box ATP-dependent RNA helicase 35       | 12,924,807–12,926,582 | 4384                  |
| TOM1-like protein 9                          | 12,928,300–12,937,724 | 0                     |
| D-amino-acid transaminase                    | 12,946,628–12,949,340 | 15,662                |
| Transcription factor MYB3R-1                | 12,951,386–12,957,121 | 20,420                |
Table S7. Bayesian estimates of the proportion of genetic variation in caterpillar performance traits explained by *M. sativa* genetics or *L. melissa* genetics as inferred from fitting Bayesian sparse linear mixed models with *gemma* that included 20 genetic PCs. Traits shown are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Posterior medians (med) and lower (lb) and upper bounds (ub) of Bayesian equal-tail probability intervals are given.

| Trait   | *M. sativa* |   |   | *L. melissa* |   |   |
|---------|-------------|---|---|--------------|---|---|
|         | med        | lb | ub | med          | lb | ub |
| W8d     | 0.11       | 0.03 | 0.23 | 0.28         | 0.19 | 0.38 |
| W14d    | 0.35       | 0.22 | 0.49 | 0.12         | 0.04 | 0.23 |
| WPup    | 0.17       | 0.02 | 0.42 | 0.05         | 0.00 | 0.19 |
| S8d     | 0.02       | 0.00 | 0.09 | 0.21         | 0.14 | 0.28 |
| S14d    | 0.03       | 0.00 | 0.10 | 0.18         | 0.13 | 0.25 |
| SPup    | 0.20       | 0.11 | 0.31 | 0.05         | 0.01 | 0.13 |
| SAdu    | 0.13       | 0.05 | 0.24 | 0.11         | 0.04 | 0.21 |
| Stot    | 0.03       | 0.00 | 0.11 | 0.19         | 0.13 | 0.26 |
| Stime   | 0.09       | 0.02 | 0.20 | 0.13         | 0.08 | 0.20 |
Table S8. Bayesian estimates of the proportion of genetic variation in caterpillar performance traits explained by *M. sativa* genetics or *L. melissa* genetics that is explained by measurable SNP-performance associations as inferred from fitting Bayesian sparse linear mixed models with `gemma` that included 20 genetic PCs. Traits shown are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Posterior medians (med) and lower (lb) and upper bounds (ub) of Bayesian equal-tail probability intervals are given.

| Trait   | *M. sativa* | *L. melissa* |
|---------|--------------|--------------|
|         | med | lb | ub | med | lb | ub |
| W8d     | 0.26 | 0.00 | 0.84 | 0.83 | 0.58 | 0.98 |
| W14d    | 0.20 | 0.00 | 0.82 | 0.30 | 0.00 | 0.86 |
| Wpup    | 0.34 | 0.00 | 0.92 | 0.35 | 0.00 | 0.93 |
| S8d     | 0.39 | 0.00 | 0.93 | 0.97 | 0.89 | 1.00 |
| S14d    | 0.34 | 0.00 | 0.93 | 0.96 | 0.83 | 1.00 |
| SPup    | 0.25 | 0.01 | 0.70 | 0.30 | 0.00 | 0.90 |
| SAdu    | 0.23 | 0.00 | 0.85 | 0.73 | 0.20 | 0.98 |
| Stot    | 0.45 | 0.00 | 0.95 | 0.88 | 0.68 | 0.99 |
| Stime   | 0.13 | 0.00 | 0.79 | 0.68 | 0.41 | 0.94 |
Table S9. Summary of genetic contributions to plant trait variation in the main Greenville Farm common garden and 2018 greenhouse experiment. PVE denotes the proportion of trait variation explained by genetic effects from the Bayesian multilocus genetic mapping model applied to the common garden experiment; posterior medians (med) and lower (lb) and upper bounds (ub) of the 95% equal-tail probability interval are given. Variance components (var) for the contribution of plant population and plant family to the trait variation in the greenhouse experiment are also given, along with restricted likelihood ratio test statistic (RLRT) and associated \( P \) values for the null that the variance component is 0. Results are shown for leaf length, leaf width, leaf area, leaf weight, specific leaf area (SLA), trichome density, plant height, leaf toughness and field herbivory levels (common garden only).

| Trait       | PVE | Plant pop. | Plant fam. |
|-------------|-----|------------|------------|
|             | med | lb  | ub  | var | RLRT | \( P \) | var | RLRT | \( P \) |
| Leaf length | 0.09 | 0.02 | 0.19 | 0.06 | 21.88 | <0.001 | 0.18 | 38.47 | <0.001 |
| Leaf width  | 0.39 | 0.28 | 0.49 | 0.09 | 32.63 | <0.001 | 0.27 | 76.36 | <0.001 |
| Leaf area   | 0.09 | 0.01 | 0.20 | 0.10 | 37.69 | <0.001 | 0.25 | 65.39 | <0.001 |
| Leaf shape  | 0.28 | 0.18 | 0.39 | 0.01 | 1.52  | 0.076  | 0.17 | 34.53 | <0.001 |
| Leaf weight | 0.34 | 0.21 | 0.46 | 0.06 | 20.92 | <0.001 | 0.23 | 58.50 | <0.001 |
| SLA         | 0.12 | 0.02 | 0.23 | 0.04 | 12.08 | <0.001 | 0.13 | 12.93 | <0.001 |
| Trichomes   | 0.20 | 0.10 | 0.31 | 0.02 | 2.85  | 0.033  | 0.18 | 36.56 | <0.001 |
| Height      | 0.28 | 0.19 | 0.36 | 0.10 | 38.24 | <0.001 | 0.37 | 130.74 | <0.001 |
| Toughness   | 0.20 | 0.10 | 0.31 | 0.00 | 0.06  | 0.326  | 0.09 | 10.68 | <0.001 |
| Herbivory   | 0.06 | 0.01 | 0.15 | NA  | NA    | NA    | NA  | NA    | NA     |
Table S10. Variance in caterpillar performance explained by plant trait polygenic scores. Results are shown for LASSO regression models of caterpillar performance polygenic scores inferred from *M. sativa* genetics and for the observed phenotypes. Variance explained is measured by $r^2$, whereas predictive variance explained is measured by cross-validation (CV) $r^2$. Caterpillar performance traits shown are W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.

| Trait  | Poly. score  | Obs. phenotype |
|--------|--------------|----------------|
|        | $r^2$  | CV $r^2$  | $r^2$  | CV $r^2$  |
| W8d    | 0.80   | 0.76   | 0.12   | 0.02   |
| W14d   | 0.61   | 0.58   | 0.07   | 0.04   |
| WPup   | 0.71   | 0.68   | 0.10   | 0.01   |
| S8d    | 0.76   | 0.73   | 0.00   | 0.00   |
| S14d   | 0.76   | 0.73   | 0.00   | 0.00   |
| SPup   | 0.72   | 0.68   | 0.09   | 0.05   |
| SAdu   | 0.71   | 0.66   | 0.06   | 0.00   |
| Stot   | 0.41   | 0.39   | 0.00   | 0.00   |
| Stime  | 0.75   | 0.71   | 0.00   | 0.00   |
Table S11. Variance in caterpillar performance explained by plant trait polygenic scores and interactions with caterpillar genetics (PCs 1-4). Results are shown for LASSO regression models of caterpillar performance polygenic scores inferred from *M. sativa* genetics and for the observed phenotypes. Variance explained is measured by $r^2$, whereas predictive variance explained is measured by cross-validation (CV) $r^2$. Caterpillar performance traits shown are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.

| Trait  | $r^2$ | CV $r^2$ |
|--------|-------|----------|
| W8d    | 0.62  | 0.48     |
| W14d   | 0.40  | 0.25     |
| WPup   | 0.48  | 0.32     |
| S8d    | 0.55  | 0.29     |
| S14d   | 0.52  | 0.26     |
| SPup   | 0.62  | 0.27     |
| SAdu   | 0.85  | 0.28     |
| Stot   | 0.34  | 0.17     |
| Stime  | 0.64  | 0.32     |
| ID  | Aglycone                        | RT    | Mass   | MS/MS | Formula   | Class  | Class Source |
|-----|--------------------------------|-------|--------|-------|-----------|--------|--------------|
| Apigenin 7-[p-coumaroyl-(→2)-[glucuronyl-(1→3)]-glucuronide] | 2.727 | 944.1856 | Y     | \(C_42H_40O_{25}\) | Flavonoid Glycoside | CFM-ID |
| Medicagenic acid 3-O-beta-D-glucoside (MESA.1112) | 3.892 | 664.3815 | N     | \(C_{36}H_{56}O_{11}\) | Saponin | METLIN |
| Peptide (MESA.1185) | 2.647 | 472.196 | Y     | \(C_{18}H_{28}N_{6}O_{9}\) | Peptide | METLIN |
| PC(P-18:1(9Z)/22:2(13Z,16Z)) (MESA.122) | 9.146 | 803.532 | N     | \(C_{46}H_{78}NO_{8}P\) | Phosphatidyl Choline | CANOPUS |
| Diglyceride (MESA.124) | 11.75 | 712.5103 | Y     | \(C_{47}H_{68}O_{5}\) | Lipids | Lipid Maps |
| \(\beta-(2-O-\beta-D-Galactopyranosyl-\beta-D-glucopyranuronosyloxy)\)-Gypsogenin | 4.212 | 1116.5345 | N     | \(C_{54}H_{84}O_{24}\) | Saponin | METLIN |
| 16-alpha-hydroxy-23-oxooleana-12-ene-28-oic acid 28-(2-O-alpha-L-rhamnopyranosyl-beta-D-fucopyranosyl) ester (MESA.1305) | 2.512 | 472.1963 | Y     | \(C_{18}H_{28}N_{6}O_{9}\) | Peptide | METLIN |
| PC (MESA.339) | 12.35 | 911.6881 | Y     | \(C_{48}H_{98}NO_{12}P\) | Phosphatidyl Choline | Lipid maps |
| \(\beta-(2-O-\beta-D-Galactopyranosyl-\beta-D-glucopyranuronosyloxy)\) Soyasapogenol A (MESA.730) | 3.367 | 944.4944 | N     | \(C_{47}H_{76}O_{19}\) | Saponin | METLIN |
| Peptide (MESA.849) | 3.925 | 249.1336 | Y     | \(C_{14}H_{19}NO_3\) | N-acyl amine | CANOPUS |
| Peptide (MESA.784) | 2.977 | 392.1101 | Y     | \(C_{15}H_{16}N_{6}O_{7}\) | Amino acid derivative | CANOPUS |
| Peptide (MESA.584) | 2.512 | 472.1963 | Y     | \(C_{18}H_{28}N_{6}O_{9}\) | Peptide | METLIN |
| Peptide (MESA.615) | 3.204 | 529.3227 | Y     | \(C_{23}H_{43}N_{7}O_{7}\) | N-acyl amine | CANOPUS |
| Peptide (MESA.545) | 2.085 | 407.1688 | Y     | \(C_{20}H_{26}N_{2}O_{7}\) | Peptide | CANOPUS |
| Fragment of MESA.615 (MESA.583) | 3.182 | 190.1359 | Y     | \(C_{13}H_{18}N_7O_3\) | N-acyl amines |
| Peptide (MESA.584) | 2.512 | 472.1963 | Y     | \(C_{18}H_{28}N_{6}O_{9}\) | Peptide | METLIN |
| Peptide (MESA.615) | 3.204 | 529.3227 | Y     | \(C_{23}H_{43}N_{7}O_{7}\) | N-acyl amine | CANOPUS |
| 3-O-beta-D-glucuronopyranosyl-28-O-[alpha-L-rhamnopyranosyl-(1→2)-beta-D-glucopyranosyl]oxy] soyasapogenol A (MESA.112) | 9.94 | 799.5293 | Y     | \(C_{46}H_{74}NO_{8}P\) | Phosphatidyl Choline | LipidAnnotator |

Table S12: Annotation of the 20 chemicals most strongly associated with polygenic scores for caterpillar performance. ID = study identifier for peak table and putative peak annotation; Aglycone = aglycone associated with saponin or flavonoid glycosides; RT = peak retention time; MS/MS = tandem mass spectra were acquired for peaks; Formula = proposed peak chemical; Class = compound class; Class Source = application or database used to classify compounds.
Table S13. Summary of associations of plant chemicals with caterpillar performance traits based on plant polygenic scores. Standardized LASSO regression coefficients are shown for the 20 phytochemicals most strongly associated with performance across the 9 performance traits. See Table S12 for full details of chemical identifications. The caterpillar performance traits are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.

| Chemical       | W8d | W14d | Wpup | S8d | S14d | SPup | SAdu | Stot | Stime |
|----------------|-----|------|------|-----|------|------|------|------|-------|
| Apigenin       | 0.00| 0.00 | 0.00 | 0.00| 0.00 | 0.05 | 0.03 | 0.00 | 0.01  |
| MESA.1112      | 0.00| 0.00 | 0.00 | 0.04| 0.04 | 0.03 | 0.02 | 0.04 | 0.06  |
| MESA.1185      | 0.00| 0.00 | 0.00 | -0.06| -0.06 | -0.04| 0.00 | -0.03| -0.06 |
| MESA.122       | 0.00| -0.05| 0.00 | 0.00| 0.00 | 0.00 | 0.00 | 0.00 | 0.00  |
| MESA.124       | 0.00| 0.00 | 0.00 | 0.00| 0.00 | 0.09 | 0.06 | 0.00 | 0.00  |
| MESA.1305      | 0.11| 0.00 | 0.00 | 0.00| 0.00 | 0.00 | 0.00 | 0.00 | 0.00  |
| MESA.1342      | 0.11| 0.00 | 0.00 | 0.00| 0.00 | 0.00 | 0.07 | 0.00 | 0.01  |
| MESA.143       | 0.00| 0.00 | 0.00 | 0.05| 0.03 | 0.01 | 0.03 | 0.00 | 0.07  |
| MESA.339       | 0.00| 0.03 | 0.10 | 0.00| -0.03| 0.00 | 0.00 | 0.00 | 0.00  |
| MESA.438       | 0.00| 0.00 | -0.00| 0.00| -0.00| -0.00| -0.11| 0.00 | -0.08 |
| MESA.545       | -0.03| -0.02| 0.00 | 0.00| 0.00 | -0.01| 0.00 | 0.00 | 0.00  |
| MESA.583       | 0.11| 0.00 | 0.00 | -0.02| -0.06| -0.06| -0.02| -0.05| -0.08 |
| MESA.584       | 0.00| -0.09| 0.00 | 0.00| 0.00 | 0.00 | 0.00 | 0.00 | 0.00  |
| MESA.615       | 0.00| -0.02| 0.00 | 0.00| 0.00 | 0.00 | 0.00 | 0.00 | 0.00  |
| MESA.730       | 0.01| 0.02 | 0.01 | 0.04| 0.02 | 0.04 | 0.02 | 0.00 | 0.03  |
| MESA.784       | -0.02| -0.03| -0.01| 0.00| 0.00 | 0.00 | -0.01| 0.00 | 0.00  |
| MESA.849       | -0.08| -0.05| 0.00 | 0.00| 0.00 | -0.00| -0.05| 0.00 | 0.00  |
| MESA.972       | 0.01| 0.01 | 0.01 | 0.00| 0.00 | 0.04 | 0.03 | 0.00 | 0.00  |
| PC 16:3_22:6   | 0.00| 0.04 | 0.00 | 0.00| 0.00 | 0.05 | 0.00 | 0.00 | 0.00  |
| Quillaic acid  | -0.02| -0.02| 0.00 | 0.00| 0.00 | 0.00 | 0.00 | 0.00 | 0.00  |
### Table S14. List of source sites for the *M. sativa* or *L. melissa* caterpillars for the 2018 greenhouse experiment at Utah State University. Site abbreviations and full site names are given, along with sample sizes for *L. melissa* and *M. sativa*. 133 *Colias eurytheme* caterpillars were obtained from the Greenville Experimental Farm in Logan, UT; 196 *Vanessa cardui* were obtained from an online supplier, Carolina Biological Supply.

| Site | Site name         | Latitude (°N) | Longitude (°W) | No. *L. melissa* | No. *M. sativa* |
|------|-------------------|---------------|----------------|------------------|-----------------|
| ALP  | Alpine, WY        | 43.17         | 111.01         | NA               | 167             |
| APLL | Pole Line Road, CA| 38.59         | 121.73         | NA               | 171             |
| AWFS | Patagonia, NV     | 39.51         | 119.90         | NA               | 162             |
| BST  | Bonneville Shoreline Trail, UT | 41.73 | 111.79 | 191 | 166 |
| BWP  | Bedworth Pass, CA | 39.78         | 120.07         | 192              | NA              |
| HWR  | Hardware Ranch, UT| 41.61         | 111.62         | 99               | NA              |
| JJT  | Jardine Juniper Trail, UT | 41.80 | 111.65 | 190 | NA |
| VIC  | Victor, ID        | 43.66         | 111.11         | NA               | 170             |
| VUH  | Verdi, NV         | 39.51         | 112.00         | NA               | 165             |
Table S15. Variance components describing the contribution of plant or caterpillar population to caterpillar performance for the 2018 USU greenhouse rearing experiment, along with restricted likelihood ratio test statistic (RLRT) and associated $P$ values for the null that the variance component is 0.

| Species     | Trait | Plant pop. | Insect pop. |
|-------------|-------|------------|-------------|
|             |       | % var.     | RLRT | $P$ | % var. | RLRT | $P$ |
| L. melissa  | 8d wgt. | 7.96% | 16.13 | $< 0.001$ | 3.99% | 14.09 | $< 0.001$ |
|             | 14d wgt. | 14.1% | 56.88 | $< 0.001$ | $\sim 0.00\%$ | 0 | 1.0 |
| C. eurytheme| 8d wgt. | 2.97% | 0.70 | 0.164 | NA | NA | NA |
|             | 14d wgt. | 9.40% | 4.29 | 0.014 | NA | NA | NA |
| V. cardui   | 8d wgt. | 10.1% | 3.44 | 0.023 | NA | NA | NA |
|             | 14d wgt. | 13.0% | 4.43 | 0.012 | NA | NA | NA |
Fig. S1. Photographs of the Greenville Experimental Farm in Logan, UT (i.e., the main common garden) (a) the Gene Miller Science Garden in Logan, UT (b) and the UNR Main Station Farm in Reno, NV (c).
Fig. S2. Histograms show the minor allele frequency distributions for SNPs in the Greenville Experimental Farm (i.e., the main common garden) for *M. sativa* (a) and *L. melissa* caterpillars reared on these plants (b).
Fig. S3. Plots show the decay of linkage disequilibrium (LD) with physical distance (in base pairs) in *M. sativa* and *L. melissa*. LD was measured as the squared genotypic correlation ($r^2$) between pairs of SNPs. We then summarized LD at different physical distances by computing median values, the 95th percentile and the 99th percentile of LD values for different distance bins (< 100 bp, 100–1000 bp, 1000–5000 bp, very 10,000 bp up to 100,000 bps, and beyond 100,000 bps).
Fig. S4. Graphical summary of caterpillar performance by caterpillar source population. Results are shown for all nine caterpillar performance traits: W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Population IDs are defined in Table S1. For weight and survival time traits (a-c, h, i) points denote trait values for individual caterpillars and boxplots show the median (center line) and interquartile range (box) (whiskers extend to 1.5 × the interquartile range). For binary survival measures (d-g), bars give the proportion of caterpillars surviving in each caterpillar population.
Fig. S5. Graphical summary of caterpillar performance by plant (alfalfa) source population. Results are shown for all nine caterpillar performance traits: W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Population IDs are defined in Table S1. For weight and survival time traits (a-c, h, i) points denote trait values for individual caterpillars and boxplots show the median (center line) and interquartile range (box) (whiskers extend to 1.5 × the interquartile range). For binary survival measures (d-g), bars give the proportion of caterpillars surviving in each plant population.
Fig. S6. Summary of Markov chain Monte Carlo (MCMC) diagnostics for the proportion of variance in performance traits explained by genetics (PVE) and the proportion of the PVE explained by measurable SNP associations (PGE). Results are shown for the nine caterpillar performance, specifically, 8-day weight, 14-day weight, pupal weight, 8-day survival, 14-day survival, survival to pupation, survival to adulthood, total survival time, and truncated survival time (in order). Panels (a) and (b) show point estimates (points) and upper bounds of the 95% confidence interval (vertical lines) for the Gelman-Rubin potential scale reduction factor, which is a measure of between chain variance relative to within chain variance; values close to 1 indicate convergence (i.e., equal between and within chain variance). See Fig. S7 for corresponding example trace plots. Panels (c) and (d) provide estimates (on a log10 scale) of the effective sample size (i.e., equivalent number of independent samples from the posterior) for PVE (c) and PGE (d) for each trait. All effective sample sizes exceeded 1000 and many were greater than 10,000 (especially for PVE).
Trace plots showing Markov chain Monte Carlo (MCMC) samples of the proportion of variation explained (PVE) by additive genetic effects for 8-day weight in *M. sativa* (a) and 8-day survival in *L. melissa* (b). Each line shows the MCMC samples from a single chain (out of 10 chains total) and is shown with a distinct color. The first trace plot is indicative of most trace plots for PVE whereas the second shows the poorest mixing (highest potential scale reduction factor, see, Fig. S6).

**Fig. S7.** Trace plots showing Markov chain Monte Carlo (MCMC) samples of the proportion of variation explained (PVE) by additive genetic effects for 8-day weight in *M. sativa* (a) and 8-day survival in *L. melissa* (b). Each line shows the MCMC samples from a single chain (out of 10 chains total) and is shown with a distinct color. The first trace plot is indicative of most trace plots for PVE whereas the second shows the poorest mixing (highest potential scale reduction factor, see, Fig. S6).
Fig. S8. Comparison of SNP posterior inclusion probability (PIP) estimates for caterpillar performance traits based on subsets of Markov chain Monte Carlo (MCMC) runs. Results are shown for the nine caterpillar performance, specifically, 8-day weight, 14-day weight, pupal weight, 8-day survival, 14-day survival, survival to pupation, survival to adulthood, total survival time, and truncated survival time (in order). Panel (a) shows the Pearson correlation between PIP estimates between independent subsets of five chains (out of the 10 total) (mean = 0.67, median = 0.9). High correlations were generally observed for performance traits with multiple strongly associated SNPs, whereas lower correlations were often observed for the subset of traits with limited overall evidence of SNP-trait associations (see Fig. 4). Panel (b) show the proportion of SNPs with mean PIP greater than 0.1 in either subset of five chains that were greater than 0.1 in both subsets. All estimates exceeded 0.6. Missing points indicate no SNPs with PIP > 0.1.
Fig. S9. The scatterplot shows estimates of the proportion of variance explained (PVE) for each of nine caterpillar performance traits based on models of plant (a) and caterpillar (b) genetics with versus without the inclusion of 20 genetic PCs to control for population structure. A 1:1 line is shown for reference.
Fig. S10. Genetic mapping of caterpillar performance with the inclusion of 20 genetic PCs to control for population structure. Manhattan plots in (a) and (b) shown posterior inclusion probabilities (PIPs) for genotype-performance associations based on M. sativa and L. melissa SNPs, respectively. Points denote SNPs with different colors and symbols for different performance traits. Only SNPs with PIPs ≥ 0.01 are depicted. Horizontal lines at PIPs of 0.1 and 0.5 are included for reference.
Fig. S11. The scatterplot shows estimates of the proportion of variance explained (PVE) for each of nine caterpillar performance traits based on models of caterpillar and plant genetics fit separately with the PVEs added (x-axis) versus a single model fit with both caterpillar and plant genetics (y-axis). A 1:1 line is shown for reference.
Fig. S12. Scatterplots summarize evidence for marginal epistasis for performance traits within *M. sativa* (a-c) and *L. melissa* (d-f). Results are shown for W8d = 8-day weight (a, d), W14d = 14-day weight (b, e), and WPup = pupal weight (c, f). Points denote log_{10} P-values for tests of marginal epistasis for SNPs (only SNPs with $P < 0.05$ are shown. Horizontal lines denote strict genome-wide significance (black line, $P < \alpha = 0.05$ no SNPs) and the top 150 SNPs with the strongest evidence of marginal epistasis (red line). The latter cutoff was used for inclusion of pairwise-epistatic effects in *gemma*. 
Fig. S13. Scatterplots summarize evidence for marginal epistasis for performance traits for *M. sativa* (a-c) and *L. melissa* (d-f) allowing for within and between species genetic interactions. Results are shown for W8d = 8-day weight (a, d), W14d = 14-day weight (b, e), and WPup = pupal weight (c, f). Points denote log_{10} P-values for tests of marginal epistasis for SNPs (only SNPs with *P* < 0.05 are shown. Horizontal lines denote strict genome-wide significance (black line, *P* < 0.05) and the top 75 SNPs with the strongest evidence of marginal epistasis (red line) for each species (150 total for both species together). The latter cutoff was used for inclusion of pairwise-epistatic effects in gemma.
Fig. S14. Plot shows survival and development of L. melissa over the course of the rearing experiment for caterpillars fed plants from the test science garden. Colored regions denote the number of individuals that were living caterpillar, pupa, adults or dead at each day post hatching.
Fig. S15. Quantile-quantile plot showing estimates of the proportion of variation explained (PVE) for each of 1750 plant chemistry traits (y-axis) versus the PVE for 1750 randomized variables each obtained by permuting one of the 1750 chemistry traits with respect to plant genetic data. A 1:1 line is shown for reference.
Fig. S16. Scatterplots show the proportion of variance explained (PVE) by plant genetics for each of 1760 plant traits in relation to the genetic correlation between each plant trait and each of nine caterpillar performance traits. Polygenic scores for the performance traits were estimates solely from the plant genetic data. Caterpillar performance traits shown are W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time. Points are colored to reflect whether they are plant chemistry traits (blue, 1750 traits) or other plant traits (brown, 10 traits). A dashed line separates positive and negative genetic correlations in each panel.
Fig. S17. Genetic correlation matrix for the nine caterpillar performance traits (lower left corner), 1750 plant chemistry traits, and 10 other (non-chemical) plant traits (top right corner) based on M. sativa genetics from the core common garden. Each colored square in the heatmap denotes the genetic correlation for one pair of traits with the color determined by the Pearson correlation (see the scale on the plot).
Fig. S18. Standardized regression coefficients from LASSO models of caterpillar-performance polygenic scores inferred from *M. sativa* genetics as a function of plant-trait polygenic scores. Results are based on 1760 plant traits and are shown for W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.
Fig. S19. Standardized regression coefficients from LASSO models of caterpillar-performance polygenic scores inferred from *M. sativa* genetics as a function of principal components (PCs) of plant-trait polygenic scores. Results are based on 1064 PCs and are shown for W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.
Fig. S20. Standardized regression coefficients from LASSO models of caterpillar-performance phenotypes as a function of plant-trait polygenic scores. Results are based on 1760 plant traits and are shown for W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, SPup = survival to pupation, and SAdu = survival to adult (no covaraites were retained for the other traits).
| Trait     | Legend |
|-----------|--------|
| W8d       | ●      |
| W14d      | ●      |
| WPup      | ●      |
| S8d       | ●      |
| S14d      | ●      |
| SPup      | ●      |
| SAdu      | ●      |
| Stot      | ●      |
| Stime     | ●●     |

Fig. S21. Plot shows the proportion of variance explained in the caterpillar performance traits by LASSO regression models with polygenic scores from 1760 plant traits as possible covariates. Black dots denote estimates for the observed data and gray dots denote estimates for 100 randomizations of each performance data set. Results are shown for W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.
Fig. S22. Standardized regression coefficients from LASSO models of caterpillar-performance polygenic scores inferred from M. sativa genetics as a function of caterpillar genotype (genetic PCs 1-4) (PC), plant-trait polygenic scores (PGS), and caterpillar genotype-plant trait interactions (PC x PGS). Results are based on 1760 plant traits and are shown for W8d = 8-day weight, W14d = 14-day weight, WPup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.
Fig. S23. Scatterplot shows the proportion of main effect (non-interaction) versus interaction covariates retained with non-zero regression coefficients from the LASSO regression models of caterpillar-performance polygenic scores as a function of the plant-trait polygenic scores and plant-trait-by-caterpillar genetic PC polygenic scores. A 1:1 line is shown for reference. Each point corresponds with one of the nine caterpillar performance traits.
Fig. S24. Standardized regression coefficients from LASSO models of caterpillar-performance trait values as a function of caterpillar genotype (genetic PCs 1-4) (PC), plant-trait polygenic scores (PGS), and caterpillar genotype-plant trait interactions (PC x PGS). Results are based on 1760 plant traits and are shown for W8d = 8-day weight, W14d = 14-day weight, Wpup = pupal weight, S8d = 8-day survival, S14d = 14-day survival, SPup = survival to pupation, SAdu = survival to adult, Stot = total survival time, and Stime = (truncated) survival time.
Fig. S25. Scatterplot shows the proportion of main effect (non-interaction) versus interaction covariates retained with non-zero regression coefficients from the LASSO regression models of caterpillar-performance trait values as a function of the plant-trait polygenic scores and plant-trait-by-caterpillar genetic PC polygenic scores. A 1:1 line is shown for reference. Each point corresponds with one of the nine caterpillar performance traits.
Fig. S26. Variance in caterpillar-performance trait values explained by LASSO regression models with versus without epistasis, that is with versus with interactions between plant-trait polygenic scores and caterpillar genetics as captured by genetic PCs. A 1:1 line is shown for reference. Each point corresponds with one of the nine caterpillar performance traits. Although some traits were better explained by the model with epistasis, we found no evidence of an overall effect across traits. Specifically, a linear model of the variance explained with epistasis versus the variance explained without epistasis had an intercept not different from 0 ($\beta = 0.008$, s.e. = 0.026, $P = 0.782$) and a slope of $-1$ ($\beta = 1.03$, s.e. = 0.381, $P = 0.031$, $r^2 = 0.511$).
Fig. S27. Proportion of caterpillars surviving to 8 days (8d), 14 days (14d), pupation (Pup.), and eclosion (Eclos.) in the 2018 greenhouse experiment at Utah State University. Results are shown for four L. melissa populations (Lm-BST, Lm-BWP, Lm-HWR and Lm-JJT), the orange sulphur (Colias eurhyme; Ce), which is an alfalfa specialist, and the painted lady (Vanessa cardui; Vc), which is a generalist that rarely feeds on alfalfa.
Fig. S28. Heatmaps show Pearson correlations across butterfly species and populations for mean 8-day (a) or 14-day (b) weight when caterpillars were fed plants from different greenhouse-grown *M. sativa*. Positive correlations indicate that consistency in plant-population effects on weight across butterfly species or populations. Results are shown for four *L. melissa* populations (Lm-BST, Lm-BWP, Lm-HWR and Lm-JJT), the orange sulphur (*Colias eurytheme*; Ce), which is an alfalfa specialist, and the painted lady (*Vanessa cardui*; Vc), which is a generalist that rarely feeds on alfalfa. All 14-day weight correlations between *L. melissa* population pairs were significantly > 0 (i.e., *P* < 0.05), along with 8-day weights for *L. melissa* HWR vs JJT, *L. melissa* BST vs *C. eurytheme*, and *L. melissa* BWP vs *V. cardui*; all point estimates of correlations were positive.
Fig. S29. Scatterplots show weight measurements for caterpillars from different butterfly species reared on the same M. sativa plant. Best fit lines are shown in each panel.
Scatterplots summarize evidence for marginal epistasis for performance traits for *M. sativa* (a-e) and *L. melissa* (f-j) allowing for within and between species genetic interactions. Results are shown for S8d = survival to 8 days (a,f), S14d = survival to 14 days (b,g), SUp = survival to pupation (c,h), SAdu = survival to adult (d,i), and Stot = total survival time (e,j). Points denote log10 P-values for tests of marginal epistasis for SNPs (only SNPs with $P < 0.05$ are shown. Horizontal lines denote strict genome-wide significance (black line, $P < 0.05$) and the top 5% of SNPs with the strongest evidence of marginal epistasis (dashed blue line) for each species. The latter illustrate that for many survival traits there is a large excess of small P-values for *L. melissa* relative to *M. sativa* for the survival traits, and more generally we see cases where suspiciously large number of P-values exceed genome-wide significance. We interpret this as evidence of inflated type-I errors.
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