Online Supplementary Material

Supplementary methods

Fitness assays

To measure female fitness, 5 females from the focal DGRP line were housed with 15 *GFP* males and 10 *bw* females in a lightly yeasted food vial (the 'interaction vial'), and allowed to interact and mate for 3 days. All flies were initially 2- to 3-day-old virgins. To measure female early-life fitness, the 5 DGRP females were moved to an 'egg collection' 20mm vial containing 8mL grape juice agar and allowed to oviposit for 24h, before being returned to their original interaction vial. The eggs were allowed to develop into L1 larvae, and the number of L1s was counted (i.e. unhatched eggs did not count towards female fitness). To measure female late-life fitness, we waited a further 8 days (tipping once into a fresh interaction vial), and replaced the old *GFP* males with 15 new 2- to 3 days-old virgin *GFP* males, and allowed the flies to interact for 3 days (note that dead DGRP females or their *bw* competitors were not replaced). The groups of DGRP females were then moved to new egg collection vials and allowed to oviposit for 24h, and we again counted the number of emerging L1s. Females were therefore aged 5-6 days at the start of the first 24h egg collection period, and 17-18 days at the start of the second 24h egg collection period.

To measure male fitness, we placed 5 males from the focal DGRP line in an interaction vial with 10 *GFP* males and 15 *bw* females. All flies were initially 2- to 3-day-old virgins. After allowing the flies to interact and mate for 3 days, we moved the *bw* females to an egg collection vial and allowed them to oviposit for 24h. The females were then transferred back to their original interaction vial with the surviving DGRP and *GFP* males. The collected eggs were allowed to develop for 24h, and a random sample of up to 200 first instar larvae was collected and scored for *GFP* as a measure of male early-life fitness. The flies were then left to age in the interaction vial for 8 days, and were tipped into a fresh vial once during this time. Then, when the DGRP and *GFP* males were 14-15 days old, the *bw* females were replaced with 15 new 2- to 3-day-old virgin *bw* females, and the flies left to interact for 3 days (dead DGRP males or their *GFP* competitors were not replaced). The females were then placed in a new egg collection vial to oviposit for 24h, and the *GFP* status of the resulting L1s was scored as a measure of male late-life fitness.

The fitness assays were run in nine blocks, and DGRP line 352 was included in every block, serving as a common reference point to improve statistical power to estimate block effects on fitness. There were 8-17 lines per block, not including line 352.

To estimate the line mean values for female early- and late-life fitness, we used the R package `brms` (Bürkner, 2017) to fit a Bayesian multivariate generalised linear mixed model with early- and life-life offspring number as the response variables, line, block, and vial as random factors (with correlated effects on each response variable), and Poisson errors. We then used the model to find the posterior predictions of the line means, on the scale of the linear predictor. This modelling approach allows us to estimate and correct for block effects, to utilise the information provided by our repeated measures of vials, lines, and blocks, and to avoid pseudoreplication. We similarly used a `brms` model to obtain corrected values for line mean male fitness, except that the two response variables were the proportion of offspring sired (rather than the number) in the early- and late-life assays, and the model used binomial rather than Poisson errors. Because we used predicted fitness values on the scale of the linear predictor (de Villemereuil et al., 2016), the line means of both male and female fitness are approximately normally distributed around zero. The predicted line means for the four fitness traits were used in all downstream analyses of the fitness data.

Genome-wide associations with fitness (GWAS)

We downloaded DGRP genotypes from http://dgrp2.gnets.ncsu.edu/, then used `PLINK` v1.90 (Purcell et al., 2007) to remove variants with a minor allele frequency below 0.05, and those with $\geq 10\%$ of missing genotypes,

and imputed missing genotypes using `Beagle` 5.4 (Browning et al., 2018). Next, we tested for associations between each variant and each of the fitness traits using univariate linear mixed models implemented in `GEMMA` (Zhou & Stephens, 2012), using the decomposed genomic relatedness matrix to adjust for population stratification. We defined the reference allele as the one that was most common across all sequenced DGRP lines, such that positive effect sizes mean that DGRP lines carrying the minor (i.e. rarer) allele have higher average fitness. We also created an LD-pruned subset of SNPs via the command `--indep-pairwise 100 10 0.2` in `PLINK.` This LD-pruned subset makes possible computationally intensive analyses using `mashr` (see Methods), and ameliorates issues of statistical nonindependence for some downstream analyses. We used the variant annotations generated by the creators of the DGRP, who used `SnpEff` (Cingolani et al., 2012) to map variants to genes and identify mutational effects.

Transcriptome-wide associations with fitness (TWAS)

Using the expression data of Huang et al. (2015) we tested for associations between the line mean expression level for each expressed transcript, and the line mean for each of the four fitness traits, to perform a 'transcriptome-wide association study' (TWAS). For each transcript-trait combination, we fit a linear model to calculate the effect size of transcript abundance on the fitness trait, as well as the associated standard error. For models involving male early- or late-life fitness, the predictor variable was the line mean expression level in male whole body RNA extracts (scaled to mean 0, variance 1), while for models of female fitness, the predictor was the scaled line mean expression level in female whole bodies. For each transcript, we also used `limma` (Ritchie et al., 2015) to calculate the average expression level (across individuals of both sexes) and the average sex difference in expression (expressed as a log ratio) for use in downstream analyses.

References

Browning, B. L., Zhou, Y., & Browning, S. R. (2018). A one-penny imputed genome from next-generation reference panels. *American Journal of Human Genetics*, 103(3), 338–348.

Bürkner, P.-C. (2017). brms: An R package for Bayesian multilevel models using Stan. *Journal of Statistical Software*, Articles, 80(1), 1–28.

Cingolani, P., Platts, A., Wang, L. L., Coon, M., Nguyen, T., Wang, L., Land, S. J., Lu, X., & Ruden, D. M. (2012). A program for annotating and predicting the effects of single nucleotide polymorphisms, SnpEff. *Fly*, 6, 80–92.

de Villemereuil, P., Schielzeth, H., Nakagawa, S., & Morrissey, M. (2016). General methods for evolutionary quantitative genetic inference from generalized mixed models. *Genetics*, 204(3), 1281–1294.

Huang, W., Carbone, M. A., Magwire, M. M., Peiffer, J. A., Lyman, R. F., Stone, E. A., Anholt, R. R. H., & Mackay, T. F. C. (2015). Genetic basis of transcriptome diversity in *Drosophila melanogaster*. *PNAS*, 112(44), E6010–E6019.

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A. R., Bender, D., Maller, J., Sklar, P., de Bakker, P. I. W., Daly, M. J., & Sham, P. C. (2007). PLINK: a tool set for whole-genome association and population-based linkage analyses. *American Journal of Human Genetics*, 81(3), 559–575.

Ritchie, M. E., Phipson, B., Wu, D. I., Hu, Y., Law, C. W., Shi, W., & Smyth, G. K. (2015). limma powers differential expression analyses for RNA-sequencing and microarray studies. *Nucleic Acids Research*, 43(7), e47-e47.

Zhou, X., & Stephens, M. (2012). Genome-wide efficient mixed-model analysis for association studies. *Nature Genetics*, 44(7), 821–824.

Legends for Supplementary Datasets

Dataset S1: This dataset (provided as a .csv file) shows the 517 transcripts that were associated with one or more of the four phenotypes, with a p-value less than 0.01). For each transcript, the table gives the gene name and Flybase ID, the chromosome, the extent of male bias in gene expression (as log fold change) and average expression level (calculated from the DGRP expression data from Huang et al. 2015, *PNAS*), and the average effect size and p-value for each fitness components (calculated using linear models relating mean expression level to mean fitness across lines).

Supplmentary tables

Table S1: Recipe for *Drosophila* food used in this study.

Ingredients	Quantity
Water	1000 mL
Dextrose	75g
Cornmeal	73g
Yeast	35g
Soy flour	20g
Agar	6g
Tegosept	17mL
Acid mix (4mL orthophosphoric acid, 41mL propionic acid, 55mL water per 100mL)	14mL

Table S2: Proportion of variance (R) in fitness explained by 'DGRP line', with associated standard errors and 95% confidence intervals estimated using parametric bootstrapping. R was calculated from univariate generalised linear mixed models of each fitness trait, which included the random effect of experimental block, and had either Poisson errors (for females) or Binomial errors (for males), using the `rpt` function from the `rptR` package for R. R approximates the broad-sense heritability.

Fitness trait	R	SE	Lower 95% CI	Upper 95% CI
Female fitness early	0.49	0.05	0.39	0.59
Female fitness late	0.45	0.06	0.34	0.59
Male fitness early	0.06	0.01	0.04	0.08
Male fitness late	0.17	0.03	0.12	0.22

Table S3: Pearson correlation coefficients between the DGRP line means (estimated using two Bayesian mixed models; one for each sex) for each pair of fitness traits. These correlations approximate the genetic correlations between each pair of fitness traits.

Variable 1	Variable 2	Pearson correlation	SE	Lower 95% CI	Upper 95% CI	p value
Female fitness early	Female fitness late	0.77	0.06	0.68	0.83	3.53e-25
Female fitness early	Male fitness early	0.23	0.09	0.05	0.39	0.011
Female fitness early	Male fitness late	0.17	0.09	0.00	0.34	0.056
Female fitness late	Male fitness early	0.32	0.09	0.15	0.47	3.37e-04
Female fitness late	Male fitness late	0.32	0.09	0.15	0.47	3.38e-04
Male fitness early	Male fitness late	0.86	0.05	0.81	0.90	3.31e-38

Table S4: This table shows variants that passed the statistical significance threshold of $p < 10^{-5}$ for at least one of the four phenotypes, in a linear mixed model GWAS implemented in GEMMA. Columns 2 identifies genes that overlap the variant, and column 3 shows the site class. Columns 4-5 show the estimated effect size of the variant on the four phenotypes (where positive values mean that the minor allele is associated with higher fitness, and negative values that the minor allele is associated with lower fitness), with the p-value in parentheses ($-log_{10}$ transformed, with significant values starred). A searchable HTML version of this table, with additional information such as full gene names, is provided in the Github code repository.

Variant	FBID	Site class	Female early	Female late	Male early	Male late
2L__10373585__SNP	FBgn0041723	Intron	0.21 (0.9)	0.33 (1.9)	0.62 (6.3*)	0.36 (2.4)
2L__10666944__SNP	FBgn0051871	Intron	0.02 (0.1)	-0.04 (0.1)	-0.49 (5.3*)	-0.31 (2.2)
2L__11155919__SNP	FBgn0032350	Upstream	0.32 (1.6)	0.22 (0.9)	0.59 (5.3*)	0.28 (1.5)
2L__1139426__SNP	FBgn0031306	Intron	0.04 (0.1)	0.04 (0.1)	0.65 (5.4*)	0.21 (0.8)
2L__11398129__SNP	__	Intergenic	-0.40 (2.9)	-0.54 (5.2*)	0.07 (0.2)	0.01 (0.0)
2L__11900442__SNP	FBgn0264815	Intron	-0.39 (5.1*)	-0.19 (1.4)	-0.10 (0.5)	-0.12 (0.7)
2L__12362698__SNP	FBgn0262475	Intron	0.11 (0.7)	0.08 (0.4)	0.41 (5.4*)	0.26 (2.5)
2L__12600320__SNP	FBgn0085424	Intron	0.13 (0.8)	0.19 (1.3)	0.19 (1.4)	0.39 (5.1*)
2L__1278985__SNP	FBgn0041097	Intron	-0.68 (6.3*)	-0.59 (4.7)	-0.15 (0.5)	-0.20 (0.8)
2L__1279083__SNP	FBgn0041097	Intron	-0.64 (5.9*)	-0.58 (4.8)	-0.12 (0.4)	-0.14 (0.5)
2L__13736785__SNP	FBgn0051813	3'-UTR	-0.04 (0.2)	-0.14 (0.9)	-0.40 (5.3*)	-0.14 (0.9)
2L__14031137__SNP	FBgn0028872	Non-synonymous coding	0.22 (1.7)	0.42 (5.7*)	0.22 (1.8)	0.28 (2.7)
2L__15469662__SNP	FBgn0266893	Upstream	-0.54 (5.2*)	-0.12 (0.5)	0.08 (0.3)	0.08 (0.3)
2L__15469663__SNP	FBgn0266893	Upstream	-0.53 (5.3*)	-0.17 (0.8)	0.08 (0.3)	0.13 (0.6)
2L__16337977__SNP	FBgn0259151	Downstream	-0.54 (5.3*)	-0.27 (1.6)	-0.33 (2.2)	-0.11 (0.4)
2L__1992654__SNP	FBgn0043539	Upstream	-0.70 (5.1*)	-0.15 (0.4)	-0.05 (0.1)	-0.04 (0.1)
2L__20590123__SNP	FBgn0266214	Intron	-0.53 (5.7*)	-0.12 (0.5)	0.02 (0.1)	0.08 (0.3)
2L__2505499__DEL	__	Intergenic	-0.29 (2.4)	-0.51 (6.7*)	-0.02 (0.1)	-0.15 (0.8)
2L__3585735__SNP	__	Intergenic	-0.57 (5.1*)	-0.22 (1.0)	0.08 (0.3)	0.03 (0.1)
2L__3958319__DEL	FBgn0051774	Intron	-0.18 (0.7)	-0.17 (0.7)	-0.57 (5.1*)	-0.34 (2.1)
2L__7327873__SNP	__	Intergenic	-0.88 (6.4*)	-0.43 (1.7)	0.23 (0.7)	0.05 (0.1)
2L__7331146__SNP	__	Intergenic	-0.92 (6.9*)	-0.36 (1.3)	0.12 (0.3)	-0.08 (0.2)
2L__7331381__SNP	__	Intergenic	-0.81 (7.6*)	-0.46 (2.5)	0.28 (1.2)	0.00 (0.0)
2L__7331966__SNP	__	Intergenic	-0.87 (5.5*)	-0.30 (0.9)	0.25 (0.7)	0.03 (0.1)
2L__7332711__SNP	__	Intergenic	-0.65 (6.0*)	-0.32 (1.7)	0.05 (0.1)	-0.12 (0.4)
2L__9468802__SNP	__	Intergenic	0.27 (2.0)	0.46 (5.0*)	-0.16 (0.8)	-0.06 (0.2)
2R__11451981__SNP	FBgn0034032	Intron	-0.34 (1.7)	-0.62 (5.1*)	-0.24 (0.9)	-0.22 (0.8)
2R__11587427__SNP	FBgn0050080	3'-UTR	-0.27 (2.2)	-0.44 (5.3*)	-0.17 (1.0)	-0.06 (0.3)
2R__13736790__SNP	FBgn0041585	Intron	-0.39 (1.3)	-0.24 (0.7)	-0.60 (2.7)	-0.84 (5.2*)
2R__14993454__SNP	FBgn0004168	Intron	-0.74 (5.2*)	-0.24 (0.8)	0.05 (0.1)	-0.04 (0.1)
2R__14993748__SNP	FBgn0004168	Intron	-0.91 (7.7*)	-0.34 (1.4)	0.15 (0.4)	-0.11 (0.3)
2R__14993888__SNP	FBgn0004168	Intron	-0.82 (6.8*)	-0.25 (0.9)	0.19 (0.6)	-0.08 (0.2)
2R__15508894__SNP	FBgn0003435	Intron	-0.10 (0.5)	-0.14 (0.9)	-0.33 (3.8)	-0.41 (5.7*)
2R__15509740__SNP	FBgn0003435	Intron	-0.03 (0.1)	-0.14 (0.9)	-0.42 (5.9*)	-0.19 (1.4)
2R__16248031__SNP	__	Intergenic	-0.75 (7.2*)	-0.27 (1.2)	0.11 (0.3)	-0.08 (0.2)
2R__16716337__SNP	FBgn0016984	Synonymous coding	-0.02 (0.1)	0.01 (0.0)	0.09 (0.4)	0.50 (6.3*)
2R__18582247__SNP	FBgn0005631	Synonymous coding	-0.63 (5.3*)	-0.23 (1.0)	0.11 (0.3)	0.11 (0.3)
3L__10151651__SNP	FBgn0052057	Intron	-0.36 (2.0)	-0.20 (0.8)	-0.61 (5.2*)	-0.42 (2.7)
3L__10301535__SNP	__	Intergenic	-0.58 (5.0*)	-0.33 (1.9)	0.04 (0.1)	-0.19 (0.8)
3L__10619878__SNP	FBgn0085267	Synonymous coding	0.10 (0.4)	-0.17 (0.9)	-0.26 (1.6)	-0.50 (5.0*)
3L__11211699__SNP	FBgn0261553	Intron	0.02 (0.1)	0.03 (0.1)	0.62 (6.0*)	0.27 (1.4)
3L__11350860__INS	__	Intergenic	-0.09 (0.5)	-0.08 (0.4)	0.13 (0.8)	0.39 (5.1*)
3L__11939100__SNP	FBgn0262401	Downstream	-0.79 (5.7*)	-0.54 (2.8)	0.18 (0.5)	0.33 (1.3)
3L__13517615__SNP	FBgn0264001	3'-UTR	-0.52 (5.0*)	-0.27 (1.6)	-0.19 (0.9)	-0.06 (0.2)
3L__1396396__SNP	FBgn0003138	Intron	-0.04 (0.1)	-0.12 (0.5)	-0.53 (5.2*)	-0.23 (1.3)
3L__18121280__SNP	FBgn0036778	Downstream	-0.29 (2.4)	-0.45 (5.3*)	-0.03 (0.1)	0.07 (0.3)
3L__20120237__SNP	FBgn0036939	Intron	-0.25 (1.2)	-0.21 (0.9)	-0.33 (2.0)	-0.54 (5.1*)
3L__2209187__DEL	__	Intergenic	-0.34 (2.4)	-0.56 (6.3*)	0.04 (0.1)	-0.03 (0.1)
3L__2327474__SNP	FBgn0035331	Intron	-0.69 (6.0*)	-0.54 (3.6)	-0.23 (1.0)	-0.10 (0.3)
3L__2327987__DEL	FBgn0035331	Intron	-0.56 (5.1*)	-0.33 (2.0)	-0.09 (0.3)	-0.14 (0.6)
3L__2328091__SNP	FBgn0035331	Intron	-0.68 (5.8*)	-0.48 (3.0)	-0.17 (0.6)	-0.11 (0.4)
3L__2579211__SNP	FBgn0010909	Intron	0.14 (0.6)	-0.09 (0.4)	-0.22 (1.3)	-0.47 (5.0*)
3L__3852986__SNP	FBgn0013751	Intron	-0.78 (5.1*)	-0.12 (0.3)	-0.09 (0.2)	0.15 (0.4)
3L__4337825__SNP	FBgn0035533	Intron	0.00 (0.0)	-0.10 (0.5)	0.15 (0.9)	0.43 (5.7*)

(continued)

Variant	FBID	Site class	Female early	Female late	Male early	Male late
3L_4717489_SNP	FBgn0035574	Intron	-0.11 (0.3)	-0.04 (0.1)	-0.40 (2.0)	-0.75 (6.4*)
3L_5974927_SNP	_	Intergenic	0.12 (0.6)	0.03 (0.1)	0.43 (5.4*)	0.17 (1.2)
3L_7709650_SNP	FBgn0261788	Intron	-0.09 (0.3)	0.04 (0.1)	0.61 (5.2*)	-0.02 (0.1)
3R_15069383_SNP	FBgn0038693	Synonymous coding	-0.47 (2.6)	-0.70 (5.3*)	0.13 (0.4)	0.09 (0.2)
3R_20857835_SNP	FBgn0039260	Synonymous coding	-0.16 (0.5)	-0.14 (0.4)	-0.43 (2.2)	-0.74 (6.0*)
3R_23465476_SNP	FBgn0266579	Downstream	-0.79 (5.5*)	-0.27 (0.9)	0.36 (1.5)	0.16 (0.5)
3R_23561601_SNP	FBgn0005659	Upstream	-0.20 (1.3)	-0.46 (5.3*)	-0.14 (0.8)	-0.09 (0.4)
3R_23561644_SNP	FBgn0005659	Upstream	-0.32 (2.3)	-0.55 (6.6*)	-0.30 (2.1)	-0.25 (1.6)
3R_26029886_SNP	_	Intergenic	-0.81 (5.4*)	-0.32 (1.1)	0.02 (0.0)	0.08 (0.2)
3R_6838975_SNP	FBgn0083950	Intron	0.27 (2.6)	0.39 (5.3*)	0.08 (0.4)	0.00 (0.0)
3R_6840122_SNP	FBgn0083950	Intron	-0.20 (1.6)	-0.39 (5.1*)	-0.08 (0.4)	0.10 (0.6)
3R_7772970_SNP	FBgn0037963	Intron	-0.66 (5.2*)	-0.27 (1.1)	0.05 (0.1)	-0.02 (0.1)
X_13282830_SNP	FBgn0030481	3'-UTR	-0.60 (5.3*)	-0.43 (2.9)	0.13 (0.5)	0.12 (0.4)
X_1556505_SNP	FBgn0000210	3'-UTR	0.03 (0.1)	0.01 (0.0)	0.39 (5.2*)	0.22 (1.8)
X_19894141_DEL	FBgn0031082	Downstream	-0.70 (5.0*)	-0.58 (3.5)	-0.07 (0.2)	-0.16 (0.5)
X_19894144_SNP	FBgn0031082	Downstream	-0.78 (5.6*)	-0.63 (3.7)	-0.07 (0.2)	-0.16 (0.5)
X_20284816_SNP	FBgn0040651	3'-UTR	-0.66 (5.2*)	-0.49 (2.9)	-0.27 (1.1)	-0.06 (0.2)
X_2319952_SNP	FBgn0052797	Upstream	-0.34 (1.9)	-0.68 (6.6*)	-0.14 (0.5)	-0.09 (0.3)
X_5435183_SNP	FBgn0263512	Intron	-0.22 (1.9)	-0.39 (5.2*)	0.06 (0.3)	-0.04 (0.2)
X_5435203_SNP	FBgn0263512	Intron	-0.25 (2.3)	-0.41 (5.6*)	0.07 (0.3)	-0.01 (0.0)
X_5536216_SNP	FBgn0259994	Intron	-0.47 (5.0)	-0.49 (5.3*)	-0.03 (0.1)	0.06 (0.2)
X_5536276_SNP	FBgn0259994	Intron	-0.38 (4.0)	-0.43 (5.1*)	0.00 (0.0)	0.04 (0.2)
X_769353_SNP	FBgn0264449	Intron	-0.21 (1.4)	-0.52 (7.5*)	-0.06 (0.3)	-0.07 (0.3)
X_8641777_SNP	_	Intergenic	-0.81 (5.4*)	-0.36 (1.3)	-0.04 (0.1)	0.08 (0.2)
X_889209_SNP	_	Intergenic	-0.75 (5.3*)	-0.32 (1.2)	-0.01 (0.0)	-0.14 (0.4)

Table S5: This table tallies the numbers of loci showing a particular relationship with fitness (rows), for various different p-value thresholds (columns). For example, 'Female early only' counts the number of loci whose genotype significantly correlated with mean female early life fitness across lines. 'Age concordant, males' counts loci whose genotype correlated with early- *and* late-life fitness in males, in the same direction, while 'Age antagonistic, males' counts loci showing significant, opposite relationships with male early- and male late-life fitness. Similarly, 'Sex concordant, early' counts loci showing a concordant relationship with early life fitness in both males and females, and 'Sex antagonistic, late' counts those showing opposing relationships with late-life fitness in males and females. All categories are mutually exclusive, such that loci are only counted towards the most specific category that applies to them. Note that this method has low power to detect loci that correlate with two or more fitness metrics, because there are two or more opportunities to make a 'false negative' error, and the power is low for any given locus (we therefore use a range of p-value thresholds, including some permissive ones, to illustrate general patterns of genetic covariance).

Relationship to fitness	p < 0.01	p < 0.001	p < 1e-04	p < 1e-05	p < 1e-06	p < 1e-07
Uncorrelated with fitness	1,154,817	1,201,180	1,206,595	1,207,278	1,207,342	1,207,353
Male early only	12,827	1,457	146	14	1	0
Female early only	12,686	1,753	251	35	7	3
Male late only	12,315	1,418	171	11	2	0
Female late only	11,512	1,421	185	19	5	1
Age concordant, females	1,743	95	8	0	0	0
Age concordant, males	875	23	0	0	0	0
Sex concordant, early	318	6	1	0	0	0
Sex concordant, late	229	4	0	0	0	0
Sex antagonistic, early	17	0	0	0	0	0
Sex antagonistic, late	13	0	0	0	0	0
Sex concordant, both ages	5	0	0	0	0	0
Sex antagonistic, both ages	0	0	0	0	0	0
Age antagonistic, both sexes	0	0	0	0	0	0
Age concordant, both sexes	0	0	0	0	0	0
Age antagonistic, females	0	0	0	0	0	0
Age antagonistic, males	0	0	0	0	0	0

Table S6: Table showing the mean and median effect size (in standard units), across all 208,987 loci in an LD-pruned subset of the total. The average effect size is close to zero, reflecting the fact that most loci have essentially zero effect on fitness. However, the mean is significantly negative (shown by the t and p statistics, from intercept-only linear models), indicating that the minor allele is most often associated with lower fitness (and the major allele with higher fitness) at loci with non-zero associations with fitness.

Fitness component	Mean (SE) variant effect	Median variant effect	t value	p
Female fitness early	-0.00168 (0.00026)	-0.00192	-6.58	4.58e-11
Female fitness late	-0.00250 (0.00026)	-0.00285	-9.63	6.02e-22
Male fitness early	-0.00161 (0.00025)	-0.00147	-6.35	2.15e-10
Male fitness late	-0.00194 (0.00025)	-0.00167	-7.74	1.00e-14

Table S7: Estimated effect sizes (or differences in effect size) for the relationship between mutation load and fitness, from a Bayesian multivariate model. The columns shown the median of the posterior, its error, and the 95% credible intervals. These estimates are plotted in Figures 4E and 4F.

Effect size or effect size difference	Estimate	Error	Lower 95% CI	Upper 95% CI
Female early-life (FE)	-0.032	0.022	-0.076	0.011
Female late-life (FL)	-0.054	0.022	-0.097	-0.010
Male late-life (ME)	-0.024	0.022	-0.066	0.019
Male late-life (ML)	-0.040	0.022	-0.082	0.003
FE - FL	0.022	0.016	-0.009	0.052
ME - ML	0.017	0.012	-0.006	0.040
ME - FE	0.009	0.028	-0.046	0.064
ML - FE	-0.008	0.029	-0.065	0.049
ME - FL	0.030	0.026	-0.021	0.082
ML - FL	0.013	0.027	-0.039	0.065

Table S8: The table tallies the numbers of transcripts showing a particular relationship with fitness (rows) for various different p-value thresholds (columns). See Table S5 for the meanings of each row. As in Table S5, all categories are mutually exclusive, such that transcripts are only counted towards the most specific category that applies to them, and the method has low power to detect transcripts that correlate with two or more fitness metrics, because there are two or more opportunities to make a 'false negative' error.

Relationship to fitness	Using p < 0.05	Using p < 0.01	Using p < 0.001	Using p < 1e-04	Using p < 1e-05
Uncorrelated with fitness	12,143	13,769	14,222	14,280	14,285
Female early only	472	123	14	1	0
Female late only	384	112	15	3	1
Age concordant, males	356	59	7	0	0
Male late only	301	76	10	1	0
Age concordant, females	292	44	3	0	0
Male early only	268	89	15	1	0
Sex concordant, early	24	5	0	0	0
Sex concordant, late	18	7	0	0	0
Sex antagonistic, early	12	2	0	0	0
Sex antagonistic, late	8	0	0	0	0
Sex concordant, both ages	6	0	0	0	0
Sex antagonistic, both ages	2	0	0	0	0
Age antagonistic, both sexes	0	0	0	0	0
Age concordant, both sexes	0	0	0	0	0
Age antagonistic, females	0	0	0	0	0
Age antagonistic, males	0	0	0	0	0

Table S9: Tabular version of the information in Figures 5A and 5B, focusing on cross-sex effects in the genome. The fourth column of the table shows the numbers of variants comprising each of the 32 coloured panels in Figures 5A and 5B. The fifth column gives these numbers as a percentage of the total number of variants, while the sixth column shows the number as a percentage among the variants that have the same association with female fitness.

Age class	Association with female fitness	Association with male fitness	Number of variants	Percentage (overall)	Percentage (given association with female fitness)
Early-life	Negative	Negative	41,947	20.07	80.29
Early-life	Negative	Weakly negative	9,075	4.34	17.37
Early-life	Negative	Weakly positive	1,096	0.52	2.10
Early-life	Negative	Positive	129	0.06	0.25
Early-life	Weakly negative	Negative	9,459	4.53	18.10
Early-life	Weakly negative	Weakly negative	31,336	14.99	59.98
Early-life	Weakly negative	Weakly positive	10,546	5.05	20.18
Early-life	Weakly negative	Positive	906	0.43	1.73
Early-life	Weakly positive	Negative	738	0.35	1.41
Early-life	Weakly positive	Weakly negative	10,950	5.24	20.96
Early-life	Weakly positive	Weakly positive	31,731	15.18	60.73
Early-life	Weakly positive	Positive	8,828	4.22	16.90
Early-life	Positive	Negative	103	0.05	0.20
Early-life	Positive	Weakly negative	886	0.42	1.70
Early-life	Positive	Weakly positive	8,874	4.25	16.99
Early-life	Positive	Positive	42,383	20.28	81.12
Late-life	Negative	Negative	42,917	20.54	82.14
Late-life	Negative	Weakly negative	8,492	4.06	16.25
Late-life	Negative	Weakly positive	745	0.36	1.43
Late-life	Negative	Positive	93	0.04	0.18
Late-life	Weakly negative	Negative	8,787	4.20	16.82
Late-life	Weakly negative	Weakly negative	32,734	15.66	62.65
Late-life	Weakly negative	Weakly positive	10,158	4.86	19.44
Late-life	Weakly negative	Positive	568	0.27	1.09
Late-life	Weakly positive	Negative	495	0.24	0.95
Late-life	Weakly positive	Weakly negative	10,381	4.97	19.87
Late-life	Weakly positive	Weakly positive	33,013	15.80	63.19
Late-life	Weakly positive	Positive	8,358	4.00	16.00
Late-life	Positive	Negative	48	0.02	0.09
Late-life	Positive	Weakly negative	640	0.31	1.22
Late-life	Positive	Weakly positive	8,331	3.99	15.95
Late-life	Positive	Positive	43,227	20.68	82.74

Table S10: Tabular version of the information in Figures 5C and 5D, focusing on cross-sex effects in the transcriptome. The fourth column of the table shows the numbers of transcripts comprising each of the 32 coloured panels in Figures 5C and 5D. The fifth column gives these numbers as a percentage of the total number of transcripts, while the sixth column shows the number as a percentage among the transcripts that have the same association with female fitness.

Age class	Association with female fitness	Association with male fitness	Number of transcripts	Percentage (overall)	Percentage (given association with female fitness)
Early-life	Negative	Negative	1,578	11.05	44.18
Early-life	Negative	Weakly negative	752	5.26	21.05
Early-life	Negative	Weakly positive	551	3.86	15.43
Early-life	Negative	Positive	691	4.84	19.34
Early-life	Weakly negative	Negative	773	5.41	21.64
Early-life	Weakly negative	Weakly negative	1,168	8.18	32.70
Early-life	Weakly negative	Weakly positive	1,043	7.30	29.20
Early-life	Weakly negative	Positive	588	4.12	16.46
Early-life	Weakly positive	Negative	532	3.72	14.90
Early-life	Weakly positive	Weakly negative	1,058	7.41	29.63
Early-life	Weakly positive	Weakly positive	1,201	8.41	33.63
Early-life	Weakly positive	Positive	780	5.46	21.84
Early-life	Positive	Negative	689	4.82	19.29
Early-life	Positive	Weakly negative	594	4.16	16.63
Early-life	Positive	Weakly positive	776	5.43	21.73
Early-life	Positive	Positive	1,512	10.58	42.34
Late-life	Negative	Negative	1,603	11.22	44.88
Late-life	Negative	Weakly negative	758	5.31	21.22
Late-life	Negative	Weakly positive	534	3.74	14.95
Late-life	Negative	Positive	677	4.74	18.95
Late-life	Weakly negative	Negative	765	5.35	21.42
Late-life	Weakly negative	Weakly negative	1,175	8.22	32.89
Late-life	Weakly negative	Weakly positive	1,053	7.37	29.48
Late-life	Weakly negative	Positive	579	4.05	16.21
Late-life	Weakly positive	Negative	540	3.78	15.12
Late-life	Weakly positive	Weakly negative	1,061	7.43	29.71
Late-life	Weakly positive	Weakly positive	1,206	8.44	33.77
Late-life	Weakly positive	Positive	764	5.35	21.39
Late-life	Positive	Negative	664	4.65	18.59
Late-life	Positive	Weakly negative	578	4.05	16.19
Late-life	Positive	Weakly positive	778	5.45	21.79
Late-life	Positive	Positive	1,551	10.86	43.43

Table S11: Tabular version of the information in Figures 5A and 5B, focusing on cross-age effects in the genome. The table shows similar information to Table S9, except that we now tabulate the number of variants that have various associations with early- and late-life fitness (separately within each sex). Note that there are essentially no variants with opposing effects on early- and late-life fitness, in either sex.

Sex	Association with early-life fitness	Association with late-life fitness	Number of variants	Percentage (overall)	Percentage (given association with early-life fitness)
Female	Negative	Negative	50,560	24.19	96.77
Female	Negative	Weakly negative	1,687	0.81	3.23
Female	Negative	Weakly positive	0	0.00	0.00
Female	Negative	Positive	0	0.00	0.00
Female	Weakly negative	Negative	1,687	0.81	3.23
Female	Weakly negative	Weakly negative	48,453	23.18	92.74
Female	Weakly negative	Weakly positive	2,107	1.01	4.03
Female	Weakly negative	Positive	0	0.00	0.00
Female	Weakly positive	Negative	0	0.00	0.00
Female	Weakly positive	Weakly negative	2,107	1.01	4.03
Female	Weakly positive	Weakly positive	48,489	23.20	92.81
Female	Weakly positive	Positive	1,651	0.79	3.16
Female	Positive	Negative	0	0.00	0.00
Female	Positive	Weakly negative	0	0.00	0.00
Female	Positive	Weakly positive	1,651	0.79	3.16
Female	Positive	Positive	50,595	24.21	96.84
Male	Negative	Negative	49,584	23.73	94.90
Male	Negative	Weakly negative	2,661	1.27	5.09
Male	Negative	Weakly positive	1	0.00	0.00
Male	Negative	Positive	1	0.00	0.00
Male	Weakly negative	Negative	2,657	1.27	5.09
Male	Weakly negative	Weakly negative	46,371	22.19	88.75
Male	Weakly negative	Weakly positive	3,218	1.54	6.16
Male	Weakly negative	Positive	1	0.00	0.00
Male	Weakly positive	Negative	6	0.00	0.01
Male	Weakly positive	Weakly negative	3,214	1.54	6.15
Male	Weakly positive	Weakly positive	46,519	22.26	89.04
Male	Weakly positive	Positive	2,508	1.20	4.80
Male	Positive	Negative	0	0.00	0.00
Male	Positive	Weakly negative	1	0.00	0.00
Male	Positive	Weakly positive	2,509	1.20	4.80
Male	Positive	Positive	49,736	23.80	95.20

Table S12: Tabular version of the information in Figures 5C and 5D, focusing on cross-age effects in the transcriptome. The table shows similar information to Table S10, except that we now tabulate the number of transcripts that have various associations with early- and late-life fitness (separately within each sex). Note that there are essentially no transcripts with opposing effects on early- and late-life fitness, in either sex.

Sex	Association with early-life fitness	Association with late-life fitness	Number of transcripts	Percentage (overall)	Percentage (given association with early-life fitness)
Female	Negative	Negative	3,523	24.66	98.63
Female	Negative	Weakly negative	49	0.34	1.37
Female	Negative	Weakly positive	0	0.00	0.00
Female	Negative	Positive	0	0.00	0.00
Female	Weakly negative	Negative	49	0.34	1.37
Female	Weakly negative	Weakly negative	3,464	24.25	96.98
Female	Weakly negative	Weakly positive	59	0.41	1.65
Female	Weakly negative	Positive	0	0.00	0.00
Female	Weakly positive	Negative	0	0.00	0.00
Female	Weakly positive	Weakly negative	59	0.41	1.65
Female	Weakly positive	Weakly positive	3,450	24.15	96.61
Female	Weakly positive	Positive	62	0.43	1.74
Female	Positive	Negative	0	0.00	0.00
Female	Positive	Weakly negative	0	0.00	0.00
Female	Positive	Weakly positive	62	0.43	1.74
Female	Positive	Positive	3,509	24.56	98.26
Male	Negative	Negative	3,550	24.85	99.38
Male	Negative	Weakly negative	22	0.15	0.62
Male	Negative	Weakly positive	0	0.00	0.00
Male	Negative	Positive	0	0.00	0.00
Male	Weakly negative	Negative	22	0.15	0.62
Male	Weakly negative	Weakly negative	3,521	24.65	98.57
Male	Weakly negative	Weakly positive	29	0.20	0.81
Male	Weakly negative	Positive	0	0.00	0.00
Male	Weakly positive	Negative	0	0.00	0.00
Male	Weakly positive	Weakly negative	29	0.20	0.81
Male	Weakly positive	Weakly positive	3,520	24.64	98.57
Male	Weakly positive	Positive	22	0.15	0.62
Male	Positive	Negative	0	0.00	0.00
Male	Positive	Weakly negative	0	0.00	0.00
Male	Positive	Weakly positive	22	0.15	0.62
Male	Positive	Positive	3,549	24.84	99.38

Table S13: A list of all the GO terms with a family wise error rate (FWER) threshold of FWER < 0.05, when testing for GO enrichment among genes with a high evidence ratio (indicating greater likelihood of being sexually concordant, as measured in the early-life fitness assay). The results imply directional, sexually concordant selection on the whole-body expression levels of genes involved in the functions listed here, such as cytoplasmic translation and peptide metabolic processes.

GO	Meaning	log10 p	FWER
GO:0002181	cytoplasmic translation	13.4	0.000
GO:0006518	peptide metabolic process	11.5	0.000
GO:0043603	cellular amide metabolic process	10.6	0.000
GO:0043043	peptide biosynthetic process	9.5	0.000
GO:0006412	translation	9.3	0.000
GO:0043604	amide biosynthetic process	7.8	0.000
GO:0034641	cellular nitrogen compound metabolic process	7.4	0.000
GO:0022613	ribonucleoprotein complex biogenesis	5.8	0.005
GO:0010467	gene expression	5.1	0.008
GO:0006364	rRNA processing	5.1	0.009
GO:0042254	ribosome biogenesis	4.9	0.016
GO:0042273	ribosomal large subunit biogenesis	4.9	0.018
GO:0016072	rRNA metabolic process	4.8	0.020
GO:0000463	maturation of LSU-rRNA from tricistronic rRNA transcript (SSU-rRNA, 5.8S rRNA, LSU-rRNA)	4.7	0.020
GO:0042274	ribosomal small subunit biogenesis	4.5	0.035
GO:0044271	cellular nitrogen compound biosynthetic process	4.5	0.036