S1 Text. Further discussion of the interchromosomal effect and correlations between recombination rate and other available DGRP phenotypes.

Interchromosomal Effect

Chromosomal inversions were first discovered in *Drosophila melanogaster* [1]. Recombination is suppressed within the inverted region, yet recombination elsewhere in the genome increases through what is known as the interchromosomal effect [2,3]. The interchromosomal effect has been repeatedly documented in Drosophila [4–6], and has also been observed in other species such as grasshopper [7] and maize [8]. A large number of the DGRP lines are either homozygous or polymorphic for a chromosomal inversion, as expected for natural North American populations of *Drosophila melanogaster* [9]. Within the DGRP, there are a total of sixteen different segregating inversions, all on the autosomes [10]. Out of the 205 lines, 93 lines contain at least one inversion.

As described in the text, our recombination rate data from the DGRP are consistent with the interchromosomal effect. Lines with inversions have significantly increased rates of recombination in the *y v* interval relative to lines with standard karyotypes (35.1 cM vs. 31.0 cM, $P < 0.0001$; t-test). This trend is echoed in the *e ro* interval (20.9 cM vs. 20.7 cM) but the difference in recombination frequency between standard and inverted karyotypes is not statistically significant ($P = 0.66$, t-test). These data further confirm the interchromosomal effect in Drosophila.

Correlation with other available DGRP Phenotypes

As a widely-used community resource, the DGRP offers a unique opportunity to examine the relationship between recombination rate and other phenotypes because a variety of phenotypes have been surveyed in this panel. Although anecdotal evidence suggests a link

between recombination rate and organismal fitness [21,22], the adaptive significance of population-level variation in recombination rate remains unknown. We find no direct evidence of a relationship between recombination frequency and fitness in the *e ro* interval but we do see a marginally significant negative correlation in the *y v* interval. The direction of this correlation is opposite of what has been previously reported in humans [22] but similar to what has been reported in Drosophila [21]. It is unclear why humans and Drosophila differ in this way, and whether this is biologically relevant or an artifact of our experimental design. Indeed, our measurement of fitness is coarse and is likely a poor indicator of organismal fitness. Previously reported estimates of longevity in the DGRP, another aspect of organismal fitness, show no significant correlation with our estimates of recombination rate in either interval (**S23 Table**; [16]). Thus, any connection between recombination and fitness based on these data should be interpreted as tenuous at best.

However, if population-level variation in recombination rate has biological significance, one might expect that recombination rate would correlate with other organismal phenotypes. We tested whether crossover rates in the *e ro* or *y v* interval (of lines with standard karyotypes) were correlated with various traits including aggression [11], behavioral response to odorants [12,13], chill coma recovery [14,15], longevity [16], nutritional and immune indices [17], oxidative stress [18], pigmentation [19], sleep phenotypes [20], startle response [14,15], and starvation stress [14,15] (**S23 Table**). The majority of correlations were weak and not statistically significant. However, for the *e ro* interval, crossover rates were significantly positively correlated with female response to citral (Spearman's $\rho = 0.20$, $P = 0.03$). For the *y v* interval, crossover rates were negatively correlated with female and male response to ethyl butyrate (Spearman's $\rho = -0.21$, $P = 0.03$; Spearman's $\rho = -0.20$, $P = 0.04$, respectively) as well as female response to eugenol (Spearman's $\rho = -0.22$, $P = 0.02$). Also in the *y v* interval, similar to the *e ro* interval, crossover rates were positively correlated with female response to citral (Spearman's $\rho = 0.21$, $P = 0.03$), male response to citral (Spearman's $\rho = 0.28$, $P = 0.004$) and also to male response

to hexanal (Spearman's ρ = 0.20, *P* = 0.04). While these correlations between crossover rate and behavioral responses to different naturally occurring odorants are statistically significant, the biological link between these phenotypes remains unclear.

The most intriguing significant correlation we uncovered is the correlation of rates of crossing over in the *e ro* interval to female survival time on paraquat-laced food (ρ = -0.25, *P* = 0.01). Paraquat can cause oxidative stress and single-base damage, often corrected through the base-excision repair pathway. Though paraquat exposure does not appear to plastically increase meiotic recombination [23], there is clearly a link between stress and recombination in Drosophila and other systems [24–29]. This correlation between recombination and resistance to the toxic effects of oxidative stress specifically in females revealed here may be reflective of the general connection between stress and recombination. Interestingly, of seven candidate genes associated with oxidative stress susceptibility/resistance in the DGRP, two overlap with candidate genes selected for this study, *CG9650* and *Eip75B* [18]. This overlap could suggest conserved players in the DNA damage repair pathway in both meiotically and mitotically dividing cells.

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