On the power to detect rare recombination events

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We read with great interest the recent work in PNAS by Bergero et al. (1) describing differences in male and female recombination patterns on the guppy (*Poecilia reticulata*) sex chromosome. We fully agree that recombination in males is largely confined to the ends of the sex chromosome. Bergero et al. interpret these results to suggest that our previous findings of population-level variation in the degree of sex chromosome differentiation in this species (2) are incorrect. However, we suggest that their results are entirely consistent with our previous report, and that their interpretation presents a false controversy.

Our population genomic results indicate that crossing over between the X and Y is rare across most of the guppy sex chromosome (2), and the report by Bergero et al. (1) is entirely consistent with this. Indeed, figure 2 of ref. 1 is strikingly concordant to figure 3 of ref. 2, especially when taking into account the fact that Bergero et al. used less stringent parameters for read mapping. We have recently expanded our analysis across related species (3), and our results show similar patterns in a sister species. Importantly, our work (3) shows that the guppy sex chromosome system is in fact far older than previously assumed, implying a persistent low level of recombination between the X and Y. Even very rare recombination events between the sex chromosomes can prevent divergence of the Y (4), explaining the homomorphy on the guppy sex chromosomes, despite their significant age.

Our previous work (2) suggested that this persistent X-Y recombination varies across populations; however, Bergero et al. (1) do not detect these differences in their data. The crucial questions are about infrequent recombination events between the X and Y and why these differ between upstream and downstream populations. Bergero et al. are unable to provide this level of granularity in their recombination estimation due to low sample sizes.

To illustrate, the estimates of X-Y recombination outside the male hotspot range from 1 in 100 to 1 in 1,000 (1, 5, 6), and we used these estimates to conduct a conservative power analysis (7). On the basis of the sample sizes Bergero et al. (1) report, and using the upper bound of recombination outside the hotspots (1/100), we estimate that the authors (1) have very low power to detect even a doubling (power = 0.07, Cohen's $h = 0.08$) or a tripling (power = 0.12, Cohen's $h = 0.15$) of the recombination rate between pairs of high- and low-predation populations. In reality, we observe (2) far more subtle differences between populations in X-Y recombination, so our power analysis is extremely conservative. Linkage mapping on small scales simply does not have sufficient power to detect these rare events.

Bergero et al. (1) admit that "Given the rarity of such events, it will be difficult to estimate if such differences really exist." We whole-heartedly concur that methods based on direct inference are not likely to work without vastly greater sample sizes. We respectfully argue that their lack of evidence for population level recombination rate variation may simply be due to lack of power to detect rare crossing-over events outside of hotspots. In other words, the absence of evidence is not evidence of absence.

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