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New Finding Interesting Hypothesis

Because they are minimally pleiotropic, mutations in gene regulatory regions may contribute disproportionately to morphological evolution. However, as work by Nagy *et al.* elegantly demonstrates, even *cis*-regulatory mutations can have pleiotropic effects.

Their study focuses on two male copulatory traits that differ between *Drosophila santomea* and a closely related species, *D. yakuba*. Specifically, *D. santomea* lacks two mechanosensory bristles that are present on the male genitalia of all other *D. melanogaster* subgroup species and has an increased number of sex comb bristles on the legs relative to *D. yakuba*. First, using a combination of QTL mapping in *D. santomea* x *D. yakuba* backcross males, duplication mapping in *D. santomea-D. melanogaster* hybrid males, and null mutants in *D. melanogaster*, Nagy *et al.* determined that the *scute* gene is a strong candidate for the loss of genital bristles in *D. santomea* males. Next, using *in vivo* tests of enhancer function, Nagy *et al.* identified a *D. santomea scute* enhancer that had both decreased activity in the genitalia and increased activity in the legs relative to *D. yakuba*. Finally, using an *in vivo* transgenic assay, Nagy *et al.* identified a single mutation that could simultaneously cause a loss of genital bristles and gain of sex comb bristles. Although the precise mechanism through which this single mutation impacts two bristle traits in opposing directions is not yet known, Nagy *et al.* suggest that the T-to-G substitution simultaneously disrupts *Abd-B* binding in the genitals (*Abd-B* is expressed in the genitals, but not legs) and alters binding of an unknown factor in the legs.

Overall, this study provides the first experimental evidence of a pleiotropic *cis*-regulatory substitution between species. Although these results are not incompatible with the longstanding argument that coding changes are more likely to be pleiotropic than *cis*-regulatory changes, they do demonstrate how regulatory pleiotropy can contribute to correlated evolution of rapidly evolving morphological structures, such as genitalia.

Key unresolved questions in this system include: what, if any, effects do these bristle traits have on male reproductive success, and does the pleiotropic mutation impact any additional fitness-related traits (e.g., female reproductive structures). Addressing these questions would provide novel insights into the extent to which regulatory pleiotropy promotes or constrains morphological evolution.

Disclosures
None declared

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