Supplementary Material

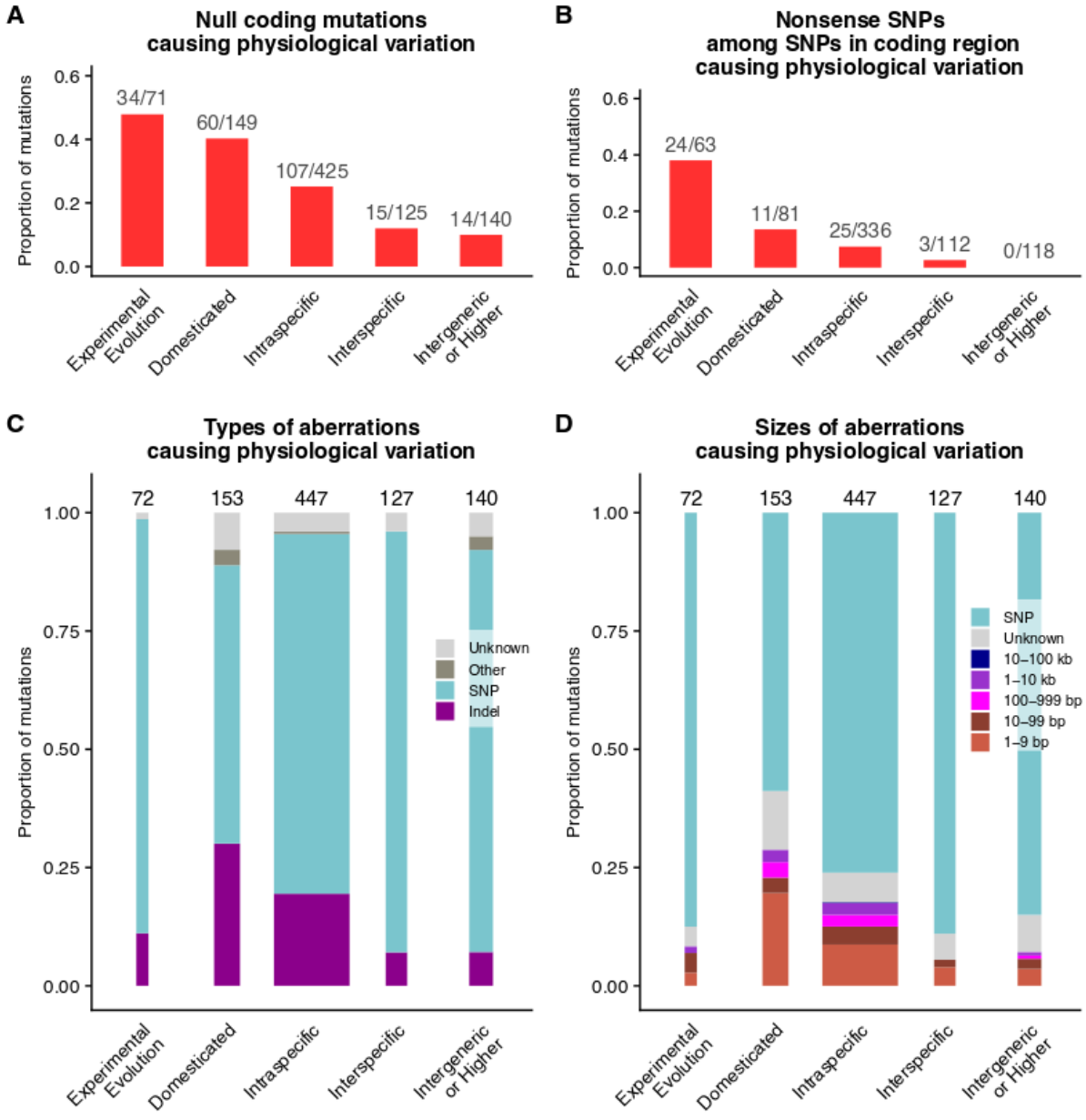

Fig. S1. The proportion of null and disruptive mutations among the coding mutations causing physiological variation decreases with evolutionary time. Same legend as Fig. 3.

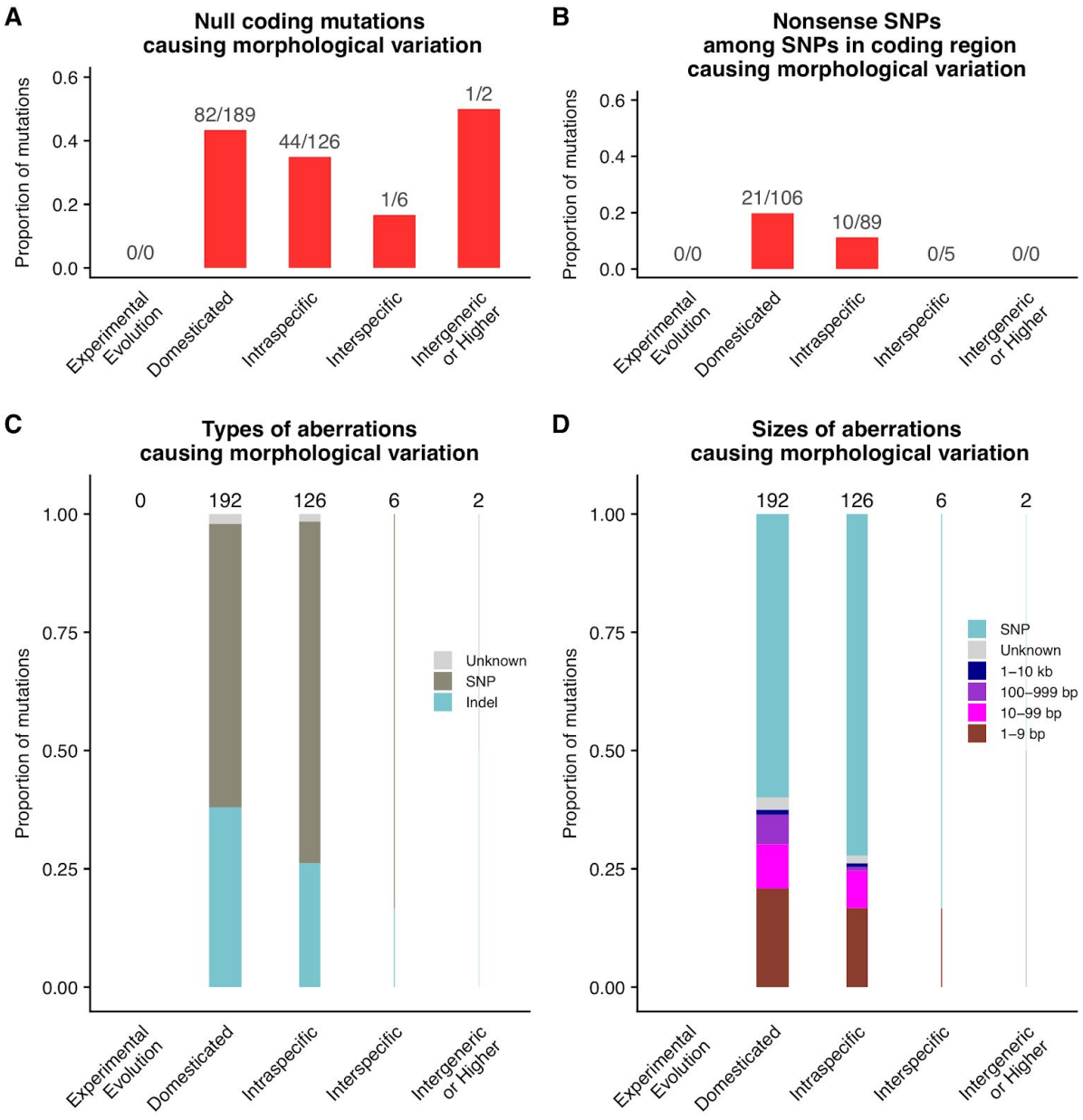

Fig. S2. The proportion of null and disruptive mutations among the coding mutations causing morphological variation decreases with evolutionary time. Same legend as Fig. 3. Cases curated as "Experimental Evolution", "Interspecific" and "Intergeneric or Higher" are too few to derive relevant estimates.

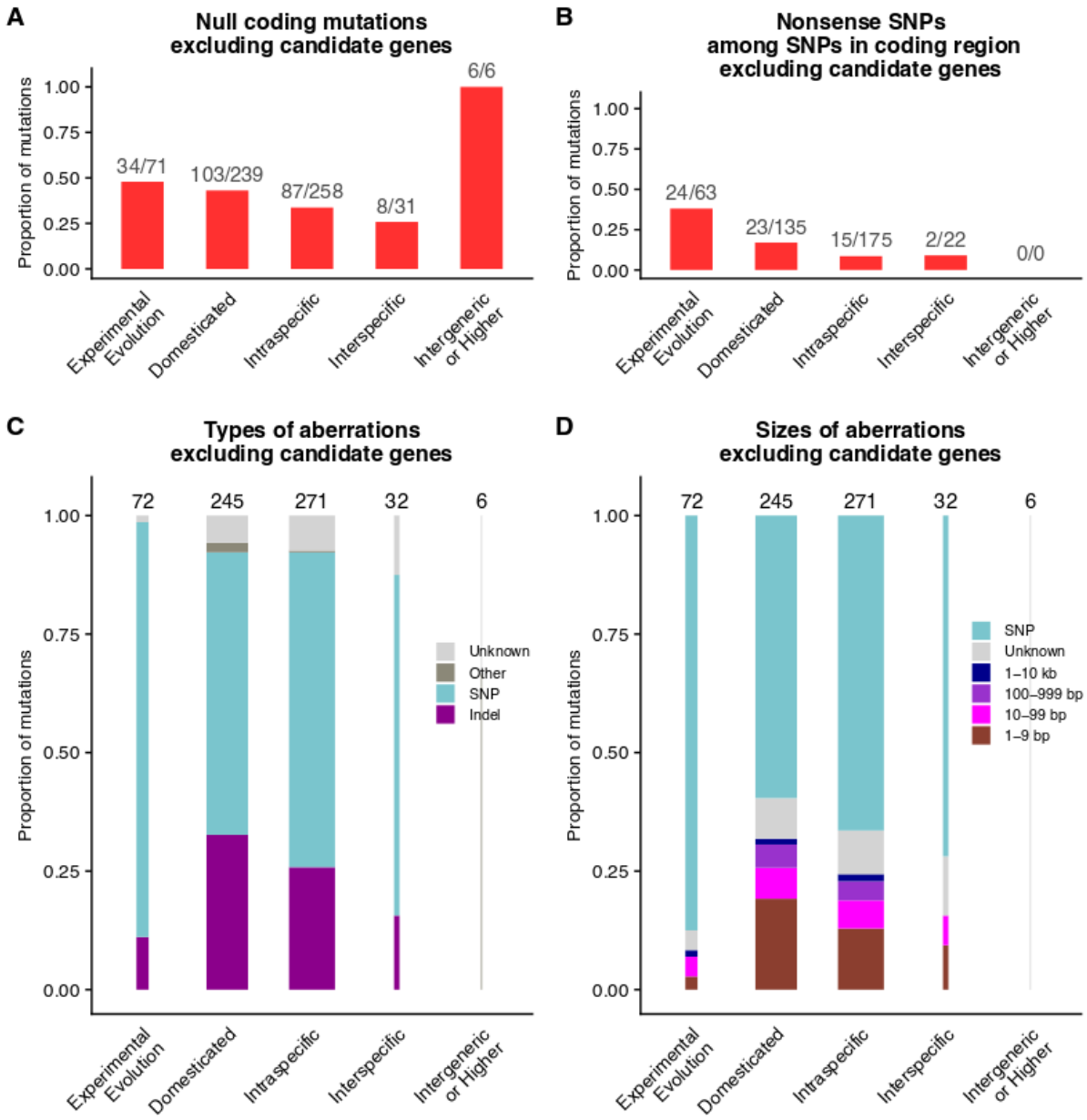

Fig. S3. The proportion of null and disruptive mutations among the coding mutations identified via methods distinct from the Candidate Gene Approach decreases with evolutionary time. Same legend as Fig. 3. The six cases curated as "Intergeneric or Higher" correspond to one study where authors performed a phylogenetic- and genome-wide screen for genes that have been inactivated repeatedly during evolution, in significant association with two metabolic phenotypes, the loss of the ability to synthesize vitamin C, and low levels of biliary phospholipids (Hiller et al., 2012).

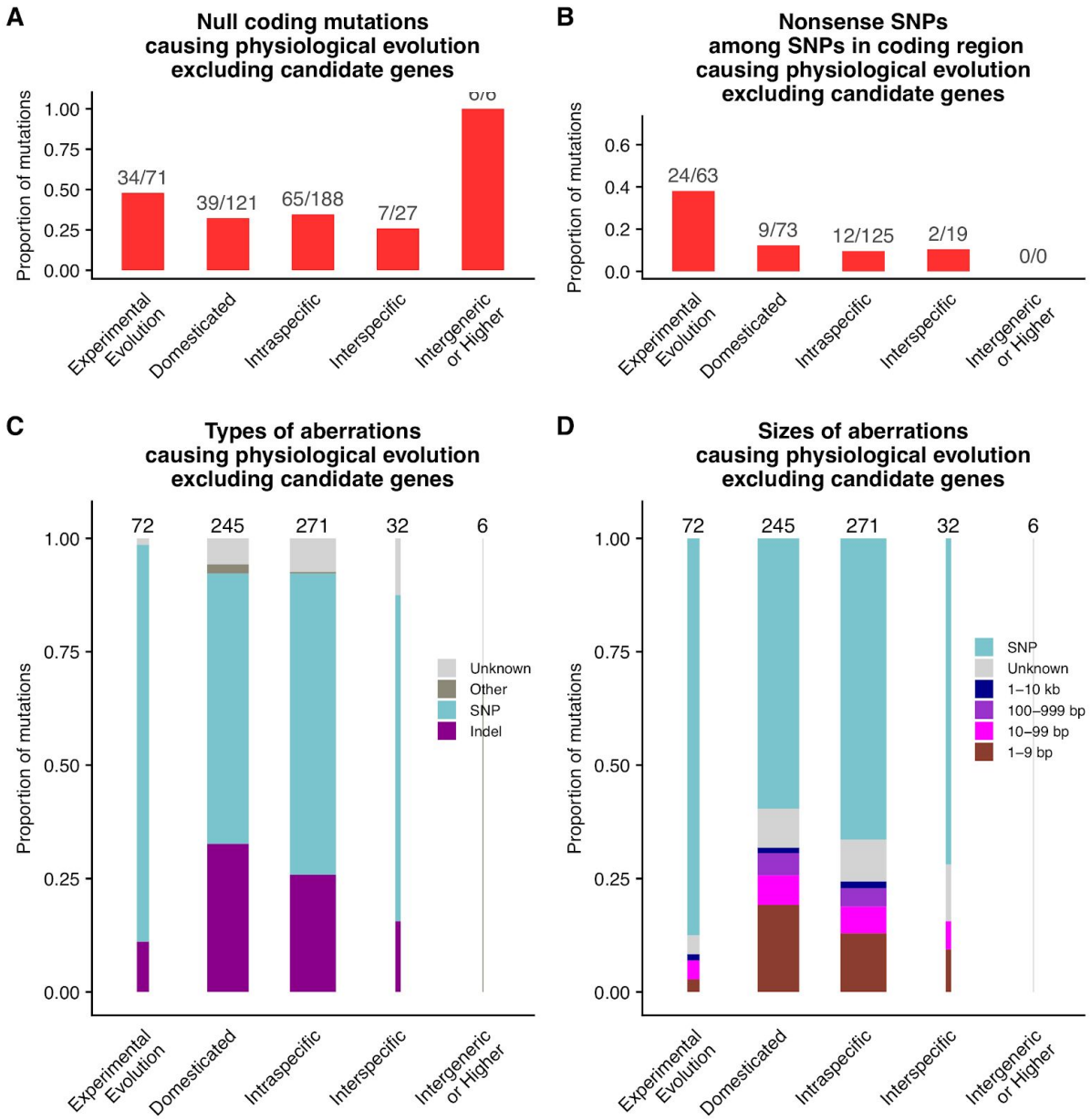

Fig. S4. The proportion of null and disruptive mutations among the coding mutations associated with physiological evolution identified via methods distinct from the Candidate Gene Approach tends to decrease with evolutionary time. Same legend as Fig. 3. The six cases curated as "Intergeneric or Higher" correspond to one study where authors performed a phylogenetic- and genome-wide screen for genes that have been inactivated repeatedly during evolution, in significant association with two metabolic phenotypes, the loss of the ability to synthesize vitamin C, and low levels of biliary phospholipids (Hiller et al., 2012).

Supplementary Reference

Hiller, M., Schaar, B. T., Indjeian, V. B., Kingsley, D. M., Hagey, L. R. and Bejerano, G. (2012). A "forward genomics" approach links genotype to phenotype using independent phenotypic losses among related species. *Cell Rep.* **2**, 817–823.

Table S1

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Table S2

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Script 1.

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