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Evolution: Anti-speciation in Walking Sticks

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The interplay between selection and genetic exchange at a color locus between populations of *Timema* walking sticks acts as an anti-speciation phenotype. This actively counteracts speciation and offers a general mechanism to explain the porous nature of species boundaries.

> "The steady and high genetic input caused by gene flow is the main factor responsible for genetic cohesion among the populations of a species."
>
> Ernst Mayr, 1963

The understanding of the origin of species, the process by which new biological species arise, has never been more within our grasp. Speciation can be due to the evolution of reproductive isolation between populations caused by adaptation to different environments (ecological speciation) [1]. Natural selection favors genetic variants advantageous for populations living in each environment, but these variants are not favoured in alternative environments. Natural selection causing adaptation to different environments therefore reduces genetic exchange and results in the formation of reproductive barriers at the same genes underlying adaptive traits, or those genes genetically correlated with them. Alternatively, species may evolve via the chance occurrence and fixation of different genetic variants between populations adapting to similar selection pressures (mutation-order speciation) [2]. Although not all species evolve by means of natural selection, the available evidence shows that most do [2,3], even when populations are free to exchange genes [4,5]. Recent experiments have confirmed that surprisingly complex genetic architectures — in terms of numbers, location and effects of genes — that contribute to speciation can arise in a remarkably short time in nature [6]. These findings are consistent with numerous examples of rapidly evolving species, from the adaptive radiation of Darwin's finches [7] to host-associated selection between hawthorn and apple host races of *Rhagoletis pomonella* [8]. However, there are a number of unexplained examples of only partial reproductive barriers between species, e.g., in pea aphids, stickleback, whitefish, butterflies and sunflowers [9–13]. In these cases, researchers have been challenged to explain incomplete speciation despite strong selection. For example, given that rapid selection is so commonplace, why are there not more species? Now, a recent paper in *Current Biology* by Comeault and colleagues [14] has a compelling and possibly very general explanation that may contribute to this phenomenon. In *Timema* walking sticks, Comeault and colleagues [14] have discovered that the interplay between natural selection and genetic architecture — the same stuff that 'good' species are made of — can also actively counteract speciation. The culprit is a coloration locus that functions as a 'genetic bridge' between divergent populations, leading to the discovery of an 'anti-speciation' phenotype in the walking sticks.

Walking the Path to Speciation

Timema walking sticks are wingless insects that inhabit southwestern North America. As its name suggests, their body shape and coloration pattern mimic its host plant environment, providing the species with an efficient, natural camouflage while they feed and mate on their host plants. *Timema cristinae* — the species studied by Comeault *et al.* [14] — uses two strikingly different host plants, *Ceanothus spinosus* and *Adenostoma fasciculatum.* *Ceanothus* is relatively large, tree-like, and broad leaved while *Adenostoma* is small and bush-like with thin, needle-like leaves. The walking sticks echo the host species they inhabit: natural selection by predators in populations that live on the *Ceanothus* plants favors green-unstriped individuals while natural selection on populations that live on *Adenostoma* plants favors a green striped phenotype (Figure 1).

Multiple experiments, including reciprocal transplants in the field, have demonstrated that these different populations are adapted to their respective hosts [15]. This system has been a goldmine for speciation research. However, persistent gene flow between adjacent populations on different hosts has raised some serious questions about the factors that maintain the connection between these populations even in the face of such strong selection. Indeed, most evolutionary studies have focused on the factors that promote speciation rather than the factors that can prevent speciation from occurring in the first place.

A Genetic Bridge

Walking stick camouflage makes for a good fit to the host plant. Yet, some walking sticks are literally the black sheep of both populations. These walking sticks are not green, but instead dark brown (melanistic; Figure 1). Melanistic forms have been dismissed as maladaptive or illustrative of the stochastic nature of selection. Comeault *et al.* [14] now tested the prediction that melanistic walking sticks may actually play an important role in preventing the formation of reproductive barriers. Unlike the color phenotypes, melanistic individuals are not under divergent selection between hosts, but are instead more cryptic to avian predators than green individuals when viewed against the dark woody stems of both host plants (Figure 1).

In addition, Comeault *et al.* [14] performed a mesocosm experiment to show that melanistic individuals are more likely to disperse onto the soil than their green counterparts. Perhaps most importantly, they discovered that melanistic individuals are more likely to mate with one another than with green forms, with data even suggesting that chemical signals commonly implicated in insect mate recognition are influencing hybridization here. Altogether, these experiments strongly support the hypothesis that melanistic phenotypes are not maladaptive, but maintained in nature by a balance of several selective forces.

If selection maintains the melanistic phenotype, one would predict lower levels of molecular divergence at the gene(s) underlying this phenotype compared to other phenotypes under divergent selection between populations. Comeault *et al.* [14] generated over 61 F1 crosses and examined segregation and inheritance patterns associated with pattern and color. The segregation patterns provided strong evidence that the melanistic phenotype was controlled by a single locus that has a major effect on melanism. In fact, the dominant 'green' allele together with the melanistic allele in this region of the genome explained almost all of the phenotypic variation in color and patterning. Further crosses and genetic mapping of these traits additionally honed in on two linked regions controlling this variation. Importantly, genome-wide estimates of molecular divergence show that this region of the genome is remarkably similar across population pairs, suggesting that melanistic individuals may provide a 'genetic bridge', across which alleles are exchanged between the two host-plant adapted populations.

Figure 1. The anti-speciation phenotype in walking sticks.
Walking stick insects (*Timema cristinae*) camouflaged on *Ceanothus* bush (top) and a visibly melanistic female (bottom). Photos by Aaron Comeault.

Speciation and Anti-speciation

Ernst Mayr [16] once mused, "a naturalist like myself has trouble with the question whether the gene or the genome is the unit of speciation. For me it is the population that is the unit of speciation (even in cases of sympatric speciation)". This is a good reminder that several ecological and evolutionary processes are at play during adaptive divergence to different environments and traits that can constrain speciation should also be considered. For example, species may evolve collectively at some traits through the spread of favorable variants (e.g., melanism in walking sticks), while diverging at other traits due to local selection (e.g., camouflage in walking sticks). Low levels of gene flow at such traits may be enough to hold populations of a species together via the spread of advantageous alleles, especially when selection coefficients are large enough to facilitate their spread and counteract the evolution of reproductive isolation [17].

Gene flow has long been considered the primary limiting factor for speciation, but the study of Comeault *et al.* [14] reveals how it is also an important contribution to understanding how the interaction between selection and gene flow can maintain genetic variation at traits within populations, thereby constraining population divergence and ultimately speciation. The *Timema* example is an important advance in speciation research and suggests that similar processes could explain the porous nature of species boundaries [18].

Of course, some evolutionary biologists will ask for more data before they are convinced of the generality of these findings. First, other evolutionary processes and interactions between them may also contribute to species cohesion (e.g., constraints from selection and genetic drift) [19]. Second, the genotypes at the color locus could not be directly observed, limiting comparisons between the color locus and SNP loci used in the genome scan. Identification of precise mutations under selection will be required for a complete understanding of the system. Yet, the genome scan was only one of many avenues of the study that supported the genetic bridge hypothesis. Finally, better empirical estimates of locus-specific migration rates and selection coefficients under different demographic scenarios will be required to fully understand the mechanism as well as the dynamics of species boundaries [20]. The evidence provided in walking sticks suggests that anti-speciation phenotypes may very well be a general phenomenon to be considered in the quest for the origin of species.

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Neurodegeneration: A Leg Up on TDP-43

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TDP-43 is a key disease protein for amyotrophic lateral sclerosis but how it drives motor neuron degeneration remains unresolved. A new study has modeled TDP-43 age-dependent axonal death in the *Drosophila* leg and used a powerful forward genetic screen to identify three novel suppressor genes.

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by adult-onset, progressive degeneration of motor neurons, resulting in rapid muscle weakness, paralysis, and death. There is compelling evidence linking the RNA-binding protein TDP-43 to ALS pathogenesis. TDP-43 is the major protein comprising the insoluble, ubiquitinated aggregates that are a hallmark of ALS neuronal pathology [1] and mutations in the gene encoding TDP-43 can also cause ALS [2]. Although it is clear that TDP-43 can regulate several aspects of RNA processing [3], how a loss of one or more of these functions, or

