

NEWS AND VIEWS**Perspective****A pheromone by any other gene would smell as sweet**Tara A. Pelletier^{1*}  | Robert D. Denton^{2*} ¹Department of Ecology, Evolution & Organismal Biology, The Ohio State University, Columbus, OH, USA²Department of Molecular and Cell Biology, University of Connecticut, Storrs, CT, USA**Correspondence**

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Reproductive isolation is the result of either the inability to produce viable and fertile offspring or the avoidance of mating altogether. While these mechanisms can evolve either over time via genetic drift or natural selection, the genetic result is usually a complex set of traits that are often linked. Explaining how reproductive isolation proceeds from the initiation of divergence to the complete prevention of mating is often a difficult task, as the underlying genes for traits associated with reproductive isolation can change via molecular evolution and subsequent protein coding alterations or through alterations of gene expression regulation. In this issue of *Molecular Ecology*, Treer, Maex, VanBoclaer, Proost, and Bossuyt (2017) use transcriptomic, proteomic and phylogenetic analyses to show that species-specific sex pheromones are the result of gradual sequence divergence on the same set of proteins in two closely related newt species (*Ichthyosaura alpestris* and *Lissotriton helveticus*). This study shows that salamander pheromone systems provide an enticing opportunity to connect the evolution of reproductive isolation to the changes in genes that underlie a key phenotype.

KEYWORDS

pheromones, reproductive isolation, salamanders, speciation

The production and interpretation of chemical signals is one of the most powerful ways for animals to establish relationships with one another, whether they be interspecific (e.g., a predator detecting the scent of prey) or intraspecific (e.g., a female assessing the quality of a male). In the latter scenario, divergence in chemical cues can provide the initiation of reproductive isolation or an important downstream mechanism in avoiding genetic incompatibility, and understanding the nature of divergence can help explain the process and timing of reproductive isolation among closely related species.

Proteins that are used for communication, such as those in pheromones, have provided examples of divergence caused by single amino acid substitutions (Leary et al., 2012), changes in sequences within biosynthetic pathways (Lassance & Löfstedt, 2013) or species-specific alterations to gene regulation (Doty, Wilburn, Bowen, Feldhoff, & Feldhoff, 2016). The sodefrin precursor-like factor (SPF) pheromone system present in salamanders is the result of multiple gene duplications, taking place throughout their diversification (Van Boclaer et al., 2015). These pheromones generally influence female receptivity, which has been demonstrated by a decrease in time to insemination

(Houck et al., 2008) and an increase in following behaviour during courtship (Van Boclaer et al., 2015). In many newt species, almost no physical contact occurs during courtship; the female uses species-specific cues from chemical signals to follow the male and pick up his spermatophore (Treer et al., 2013; Van Boclaer et al., 2015).

Treer et al. (2017) take a multifaceted approach to understand the mechanisms of evolution of the SPF complex in two closely related newt species that show no evidence of hybridization (Figure 1). Transcriptome and protein data showed that both species express a wide spectrum of SPF proteins during courtship and that transcriptome data were sufficient as a proxy for protein abundance. This determination allows for the most interesting results from this study: (i) the phylogenetic reconstruction of SPF sequence data indicates that at least ten ancestral SPF precursors existed via gene duplications before the split of these two salamander species (*Ichthyosaura alpestris* and *Lissotriton helveticus*), and (ii) species specificity in these salamanders is the likely result of gradual sequence divergence over time, not regulatory changes that alter gene expression.

Both sexual and natural selections are complex processes that change over space and time, making it difficult to predict and correctly identify a strong signal (Cornwallis & Uller, 2010). Results from

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this study, and previous results from this research group, are disentangling the evolution of a complex of sex-specific pheromones in salamanders. Using a comparative approach, as in this study between the two closely related species, we have learned that interspecific variation is the result of sequence evolution and not regulatory changes in the expression of these sequences. Importantly, this shows that even small changes in sequence evolution could place two species on a divergence path. Placing the evolution of SPF proteins in the broader context of a salamander phylogeny, we learned that gene duplications in this complex of proteins have happened multiple times over the course of millions of years and play an important role in maintaining reproductive isolation among species.

Pheromone as a tool for communication among animals, though ubiquitous, is far less studied compared to other forms of communication, especially across vertebrate taxa (Symonds & Elgar, 2008). A noteworthy aspect of chemical cues is that animals can either perceive a chemical cue or not, as opposed to visual or auditory cues that can be perceived at a wide range. This means that even small changes in the chemical component of a pheromone can have large effects, and as groups of closely related species should be using the same general biosynthetic pathways, as seen here, we might expect species that are more closely related (i.e., sister species) to have more divergent chemical compositions than others from the same Genus or Family because more distantly related species are less

likely to interbreed (Symonds & Elgar, 2008). Extending studies such as this to other species with differing levels of divergence will help disentangle the extent to which sex pheromones diverged before or after speciation, why some species use multicomponent blends and some do not, how ecological factors play a role in the evolution of these blends, and how receiver response (i.e., receptor genes) guides the evolution of sex pheromones involved in speciation.

AUTHOR CONTRIBUTIONS

Both authors contributed equally to the planning, writing, and editing of this manuscript.

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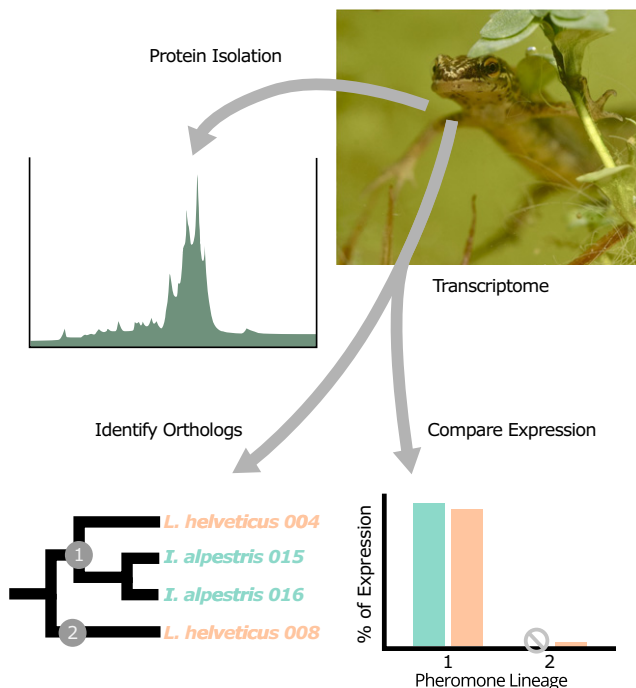


FIGURE 1 Conceptual diagram showing the linkage between isolating the major protein complex of salamander pheromones and investigating two potential routes to the diversification of this key trait under sexual selection. Clade 1 represents orthologous genes between two salamander species, and clade 2 represents a sequence unique to *Lissotriton helveticus*. While one species may display novel sequences, the majority of expressed genes map to orthologs shared between species. Figure modified from Treer et al. (2017) and photograph of *L. helveticus* courtesy of Franky Bossuyt

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