# Predators Make (Temporary) Escape from Coevolutionary Arms Race

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doi:10.1371/journal.pbio.0060075.g001

***Thamnophis sirtalis* eating a tetrodotoxic *Taricha granluosa* (Yachats, Oregon, United States). (Photo: Edmund D. Brodie III)**

Arguably cute and spanning at most 20 cm from head to tail, the rough-skinned newt packs pretty near the most poisonous punch known to the animal kingdom. *Taricha granulosa*, like all species in its genus, exudes an exceptionally potent neurotoxin, tetrodotoxin (TTX) from its skin glands. Some *Taricha* newts could wipe out thousands of mice or a clutch of humans with their toxic issue. But why produce enough poison to kill a potential predator several times over? To discourage the one predator—the common garter snake (*Thamnophis sirtalis*)—that's resistant enough to the poison to count on newts as a food source.

The toxin causes paralysis and respiratory failure by binding to sodium channels in nerve and muscle membranes and blocking the propagation of electrical signals that are necessary for proper communication between cells. The garter snake's resistance comes from structural alterations in its sodium channels that inhibit the toxin's binding capacity and deadly effects. In a classic example of a coevolutionary arms race, the resistance of the snake places selective pressure on the increasing toxicity of the newt, which in turn drives increasing resistance in the snake. But in a new study, Charles Hanifin, Edmund Brodie, Jr., and Edmund Brodie, III, show that even the most potent toxin on Earth proves no defense against garter snakes that have managed to escape from this coevolutionary tit for tat by developing extreme resistance to the newt's toxin.

Coevolution is driven by reciprocal selection arising from ecological interactions between species, which are mediated by specific traits—toxicity and resistance (newt and snake), virulence and immunity (parasite and host), beak morphology and flower shape (pollinator and plant)—known as the "phenotypic interface." The potential for reciprocal selection should be strong, conventional wisdom holds, when performance at the phenotypic interface is roughly even, because individuals will have varying abilities and thus have variable fitness consequences on each other. If the traits are mismatched—for example, the most resistant snake can still eat the most toxic newt—then individuals won't experience variable fitness costs related to these traits, which means no selection and no evolutionary response.

Increasing evidence suggests that mismatched traits between predator and prey may be fairly common and may reveal geographic variations in coevolutionary selection. In areas where newts are nontoxic (or don't exist), for example, snakes aren't resistant to TTX. To gain insight into newt–snake selection dynamics and coevolutionary trajectory—escalation, equilibrium, or de-escalation—the researchers sampled 383 newts from 28 sites spanning 2,000 km, across the pair's overlapping range, from British Columbia, Canada, to Southern California, United States, in areas where the Brodies had previously measured garter snake resistance with another colleague. The researchers estimate snake resistance based on an animal's crawling performance after an injection of varying amounts of TTX, which can impair a snake's ability to move—a clear fitness cost if the snake can't escape its own predators.

Across this range, the average per-newt toxicity varied from no measurable toxin to 4.69 mg TTX (a 2-mg dose can kill a human), closely tracking the resistance levels of local snakes. Newts with the highest toxicity tended to occur in areas inhabited by snakes with the highest resistance. However, when the researchers analyzed the phenotypic interface of these traits to see if newt toxins could threaten the fitness or survival of snakes, and vice versa, they found potential mismatches across most of the pair's geographic range. In each of these cases, snakes were resistant enough to survive a newt meal with minimal effects, thus escaping selection resulting from prey toxicity, but newts never produced enough poison to thwart ingestion. Even the most toxic newts had the misfortune of sharing their habitat with highly resistant snakes. Based on estimates of snake performance after eating a newt, the researchers concluded that newts did not produce variable effects on their predators—their toxic defense failed to compromise snake fitness or survival.

While the overall pattern of mismatches suggests a dynamic of escalating weapons and defenses driven by reciprocal selection, predators in some locations managed to escape this escalation by evolving far higher resistance than necessary to safely ingest local newts. With just a single mutation responsible for the evolution of extreme resistance in one of the mismatched snake populations, allowing for rapid spread through the population, it may be that newts simply can't synthesize deadlier toxins at the same pace.

In an earlier study, the researchers concluded that elevated predator phenotypes signaled "intense coevolution," but these results challenge that assumption. This "directional asymmetry," favoring the predator, also challenges the theoretical prediction that coevolutionary escalations should favor defensive adaptations in prey as a result of stronger selection pressure. Whether these results reflect an unusual dynamic for pairs involving toxic prey or the unique biology of the newt–garter snake interaction remains a question for future study. One thing is clear, however: evidence of the ecological interactions of predator and prey prove once again that real-life evolutionary dynamics of interacting species are far more complicated than the neatly intuitive framework laid out in theory. You can learn more about the garter snake–newt interaction at http://www.teachersdomain.org/resources/tdc02/sci/life/evo/toxicnewts/index.html.

**Hanifin CT, Brodie ED Jr, Brodie ED III (2008) Phenotypic mismatches reveal escape from arms-race coevolution. doi:10.1371/journal.pbio.0060060**