

FALL 2025

microcosm

PUBLICATION OF THE AMERICAN SOCIETY FOR MICROBIOLOGY



ANIMAL MICROBIOLOGY



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Microbes shape the lives of animals in profound ways. Aligning with the launch of ASM's new journal, [ASM Animal Microbiology](#), the Fall 2025 issue of *Microcosm* explores how insights into animal-microbe interactions are driving progress in conservation, public health and scientific innovation. With story topics ranging from antimicrobial resistance in pets to applications of the vibrio-squid symbiosis, this issue sheds light on the complex and vital relationships between animals, microbes and the people and environments with which they interact.

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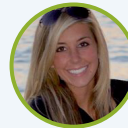
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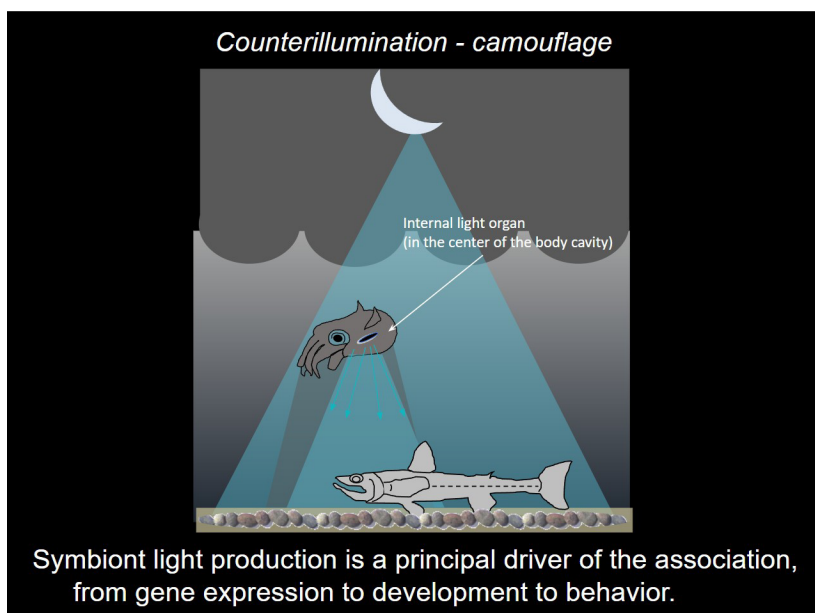
Shedding Light on the Vibrio-Squid Symbiosis

BY JENNIFER TSANG, PH.D.

For the past 20 years, [Michele "Nish" Nishiguchi, Ph.D.](#), has regularly made trips to Australia in search of Australian bobtail squid. Collecting the squid—and shipping them back to the lab—is no easy task. Nishiguchi, a professor of molecular and cell biology at University of California, Merced, has encountered venomous catfish and torpedo eels, and evaded saltwater crocodiles by carefully planning her collection sites and times. [Mark Mandel, Ph.D.](#), professor and Vice Chair of Medical Microbiology and Immunology at the University of Wisconsin-Madison, goes to Hawaii twice a year to collect Hawaiian bobtail squid. "We usually ship about a dozen or so adults [back to the lab]," he said, noting the squid will yield more than 5,000 hatchlings—each about the size of a fruit fly—over 4-5 months.



Scientists from the Mandel Lab collect Hawaiian bobtail squid at low tide in Oahu. Source: Mark Mandel, Ph.D.



V. fischeri shines light to minimize shadows cast by bobtail squid. Source: Margaret McFall-Ngai, Ph.D.

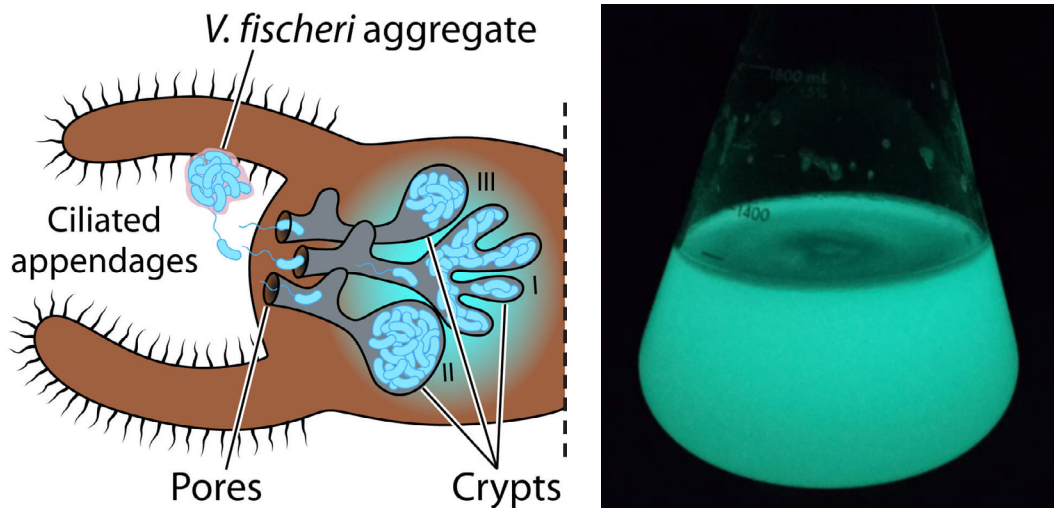
Tucked away in the squid's light organ, the bacteria produce a blue-green glow. For the squid, this bioluminescence is a matter of survival; the bacteria help shield them from predators at night by emitting light when the bacteria reach a critical mass in the squid's light organ. This light matches the moonlight above, masking the shadow that would otherwise be cast on the ocean floor, and helping to hide the squid from predators below. In return, *V. fischeri* receives nutrients and shelter.

How *V. fischeri* gets into the light organ—and how it is maintained there—is a complicated process. Yet, microbiologists find that this symbiosis, which is highly specific and experimentally tractable, serves as a powerful system for uncovering how microbes communicate with their hosts and adapt to their environment.

A COMPLEX COLONIZATION

The partnership between squids and *V. fischeri* is a multi-step process that begins after the squid first hatches. Squid hatchlings acquire *V. fischeri* from the surrounding water. "When the squid pumps oxygenated water through its mantle cavity for respiration, environmental bacteria come along with it," Mandel explained. Exposure to peptidoglycan released in the environment triggers the production of mucus from the ciliated surfaces on both sides of the squid's body. According to [Margaret McFall-Ngai, Ph.D.](#), a faculty associate at Caltech and a staff researcher at Carnegie Science, the squid "shed a huge amount of mucus." Bacteria stick to the mucus, which contains antimicrobials. These antimicrobials kill off most other bacteria but leave *V. fischeri*, which is uniquely resistant to their effects, unaffected.

Once inside the squid, the bacteria navigate a maze of pores, ducts, an antechamber and a long, narrow bottleneck before finally settling into the crypts of the light organ. McFall-Ngai said that most of the time, only 1 bacterium gets into each crypt. The reason is that the bottleneck is just wide enough for bacteria to single-file through. Once a bacterium colonizes, the bottleneck constricts, shutting out other bacteria. The bacteria begin to multiply in the crypt, and according to McFall-Ngai, the squid are completely colonized by somewhere between 12-15 hours.



Left: *V. fischeri* travels into the light organ and can completely colonize it within 12-15 hours.

Right: *V. fischeri* bioluminescence occurs at high cell density.

Source: (Left) Adapted from Fung B.L., et al./*Journal of Bacteriology*, 2024. (Right) Septer A.N. and Visick K.L./ *Journal of Bacteriology*, 2024

NOT JUST ANY VIBRIO CAN COLONIZE

Since just 1 bacterium colonizes each of the squid's 6 crypts, it's important for the squid to harbor only the brightest bacteria. Indeed, bacteria that don't produce light [don't colonize squid as well](#) as their wild-type counterparts. "The squid knows that they're dark and spits them out," Nishiguchi said.

She has seen this play out in [experimental evolution experiments](#) in which her lab has evolved *V. fischeri* strains to colonize squid from different habitats. Some of the genes that were affected during experimental evolution experiments were those involved in biofilm formation and light production. "That's something that the squid is really selecting for," she said. "They're culling out ones that they don't want in there."

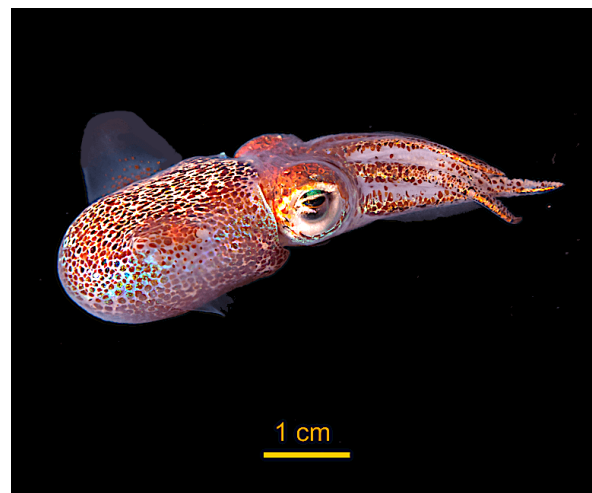
This culling happens every morning at dawn when the bobtail squid expels 90-95% of the bacteria from its light organ. At these low numbers, the bacteria don't bioluminesce because light production occurs via a density-dependent process called [quorum sensing](#). This isn't problematic for the squid since they're largely hidden and inactive during the day. Only after the bacteria reach higher densities, as they do toward nightfall, will they begin to glow.

Read: 'How Quorum Sensing Works'

A MICROCOSM OF ANIMAL-MICROBE INTERACTIONS

Research into the vibrio-squid symbiosis is useful not just for understanding squid survival, but also for answering fundamental questions about how animals and microbes interact with each other. Animal-microbe interactions are ubiquitous, ranging from symbiotic relationships, microbiomes or pathogenic interactions. In these interactions, each party is influenced by other parties and the environment they share.

While gut microbiomes are extremely complex in that they harbor [hundreds of species](#), the squid's light organ only contains a single species. This is an advantage for experimental studies. "It's like being in conversation with just 1 or 2 folks versus a whole party," said Nishiguchi. This contrasts to a complex microbiome where the microbes are responding to each other and the host at the same time. For the vibrio-squid system, its simplicity allows researchers to manipulate the interaction, and observe the outcomes, by making mutants. "[The vibrio-squid model] is really a great symbiosis because there's 1 host and 1 microbe, and we can get high resolution when we ask a question," McFall-Ngai explained.



The Hawaiian bobtail squid is a popular model organism to study vibrio-squid symbiosis, which lends insights into animal-microbe interactions on a broad scale. Source: Margaret McFall-Ngai/Wikimedia Commons via a CC BY-SA 4.0 license

For Mandel, he sees the vibrio-squid interaction as a model for understanding microbiome development. "One thing we really want to get a sense of is what are the rules of the road for how an animal gets its microbiome," he said. He added that while we know a lot about the signals that are being exchanged between squid and the bacterium, we don't quite understand the entire conversation that establishes the bacterium as a symbiont. For example, microbiologists know that biofilm formation is required for colonization, but the role of aggregation within the host is less clear.

For an animal to establish its microbiome, bacteria first interact with the host epithelial surface. McFall-Ngai points out an interesting connection between gut microbes and *V. fischeri*. "[*V. fischeri*] associates with the host in a very similar way to how bacteria associate with our gut epithelia," she said. For instance, the crypts of the gut are similar to the crypts in the light organ, and both gut microbes and *V. fischeri* secrete outer membrane vesicles that then affect distant regions in the host. "Animals evolved in the oceans that had lots of bacteria, so there's nothing older in animal evolution than the interactions of bacteria with the apical surfaces of the animal epithelia," said McFall-Ngai. Therefore, interactions between microbes and surfaces such as the gut, airways, reproductive tract and the squid's light organ are very similar and evolutionarily conserved—we can learn a lot about the former by studying the latter.

AN EARLY WARNING SYSTEM OF ENVIRONMENTAL CHANGES

Beyond helping us understand the microbiome, Nishiguchi said that beneficial microbes such as *V. fischeri* can act as "canaries in a coal mine. [Microbes are] the ones that are going to respond first, and quickly, to any kind of environmental change, such as [climate change](#)." Since microbes can divide rapidly, they adapt on a genetic level more quickly than animals that have longer reproductive timelines.

Scientists can leverage these quick microbial responses to monitor changes in a given environment, such as changes to water quality. One application of this already in play is the [Microtox](#) system, which uses *V. fischeri* to detect chemical contaminants in the water supply. The microbes emit light when healthy but exposure to toxic compounds decreases the amount of bioluminescence from the bacteria in a dose-dependent manner.

These are only a few examples of the [critical role of microbes on the lives of animals](#) and how scientists can learn about microbe-animal interactions more broadly from a 1 host-1 symbiont system. "Not every animal has symbiosis, but all animals thus far studied grew up in a microbial-rich soup," said McFall-Ngai. "[Microbes] have been foundational in shaping the biology of all animals and plants."

Do you study animal-microbe symbioses? ASM's new journal *ASM Animal Microbiology* is dedicated to disseminating high-quality and authoritative studies on animal-associated microbes and their impact on animal and public health.

[Submit a Manuscript](#)

BAIT BOXES FOR RODENTS: BREAKING THE *B. BURGDORFERI* TRANSMISSION CYCLE

With that in mind, scientists are developing targeted strategies to minimize *B. burgdorferi* infections in mice, including topically treating animals with tick-targeting chemicals, or baiting them with edible pellets containing pesticides, antibiotics or vaccines. Because white-footed mice tend to stay within a defined area of 0.1-1 hectares (0.25-2.5 acres), strategic placement of bait stations can target most mice living within that area on a residential property.

BAIT-BOXES WITH TOPICAL ACARICIDES

[Topical application of selective insecticides that kill ticks and mites \(acaricides\)](#) involves luring animals into a bait box where they either brush their fur against acaricide-treated surfaces or pick up treated nesting material.

Topically applied acaricides, like permethrin or fipronil, kill ticks attached to or attempting to attach to a rodent by targeting the insects' nervous system or other vital functions. Once applied to mice, permethrin remains biologically active on the host for about 3-4 weeks, while fipronil has a longer residual activity of 4-6 weeks.



Acaricides applied to the fur of white-footed mice kills ticks attached or attempting to attach to the rodents.
Source: Charles Homler/Wikimedia Commons via a CC BY-SA 3.0 license

The overall advantage of acaricides is that they can limit the number of larvae and nymphs completing their blood meal on the target rodent, decrease the prevalence of ticks and rodents harboring *B. burgdorferi* and reduce the number of host-seeking (questing) ticks more broadly. Because there are fewer ticks that can reproduce, the population of new nymphs—key spreaders of *B. burgdorferi*—will be reduced in the next life cycle.

One commercial product ([Damminix](#)) uses cotton-based permethrin for nesting material. A study in a wooded residential environment demonstrated that, compared to control (untreated) areas, the product resulted in [27.6% and 20.3% control of questing nymphs](#) at 1 and 2 years post-intervention, respectively. In the same study, another system ([SELECT TCS](#))—in which a treated wick is placed in a bait box, transferring acaricide to mice as they enter the box—achieved 84% and 79.1% control of host-seeking nymphs after 1 and 2 years, respectively.

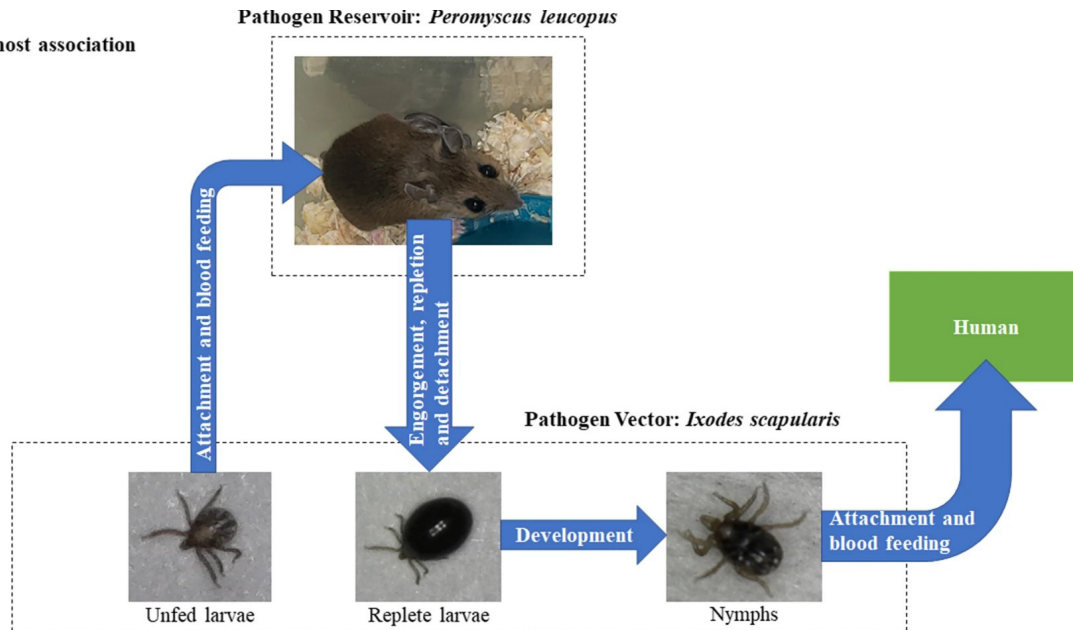
FOOD-BAIT LACED WITH ACARICIDES, ANTIBIOTICS OR VACCINES

Another approach involves integrating [acaricides, antibiotics or vaccines](#) directly into mouse food-bait.

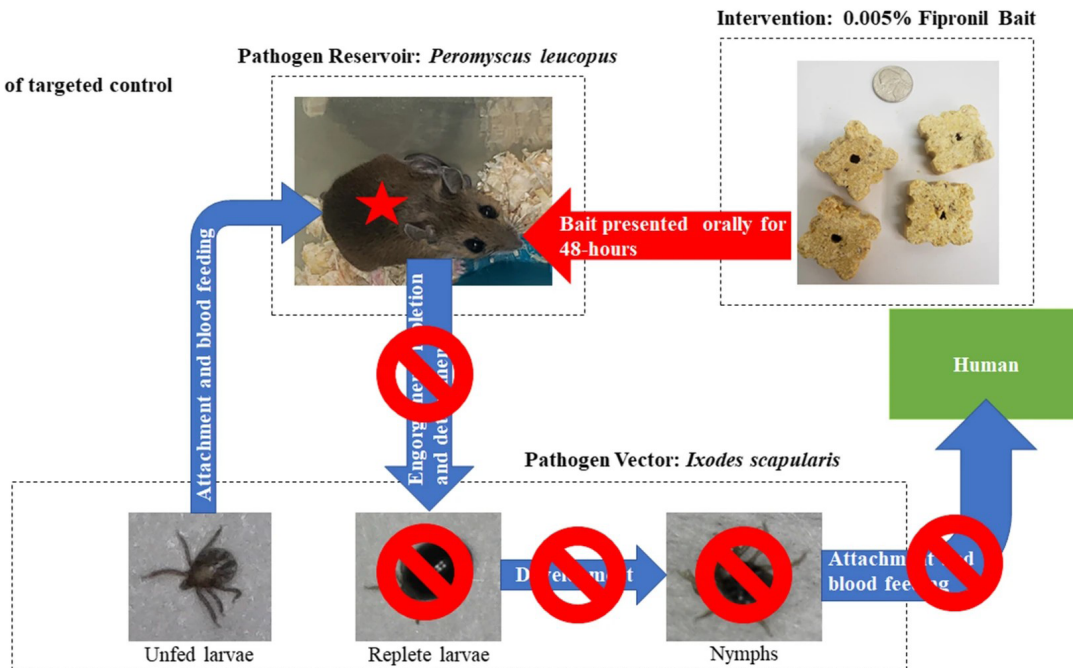
FOOD-BAIT WITH ACARICIDES

Orally delivered acaricides are commonly used in dogs, but not commercially available for use in rodents. [Lab studies with 0.005% fipronil bait](#) presented to white-footed mice indicated that the low dose application of fipronil could effectively control blacklegged tick larvae. The larvae were manually applied to treated and untreated mice, then collected after detaching from the mice. The fipronil provided 100% control of larvae that tried to attach up to 15 days post-treatment. Larvae on treated mice cannot feed to repletion or detach and eventually die.

a Vector-host association



b Impact of targeted control



White-footed mice are key reservoirs of pathogens like *B. burgdorferi*, which can be passed to ticks during feeding. Food-bait containing acaricides, like fipronil, can disrupt transmission of the bacteria.
Source: Poche D.M., et al./*Parasites & Vectors*, 2020 via a CC BY 4.0 International license

The efficacy of oral acaricides can decline over time, as drug levels in the rodent host decrease. In a lab study, *Peromyscus maniculatus* mice (deer mice) were offered peanut butter bait laced with 2 different concentrations of fluralaner (another oral acaricide) and then larvae of blacklegged ticks were placed on the mice. On day 2 post-feeding, 97% and 94% of the ticks were killed in the 50 mg/kg and 12.5 mg/kg fluralaner groups. On day 28, the efficacy was only at 3% and 4% respectively. More research is needed to understand how to overcome this limitation.

FOOD-BAIT WITH ANTIBIOTICS

Orally delivered antibiotics (e.g., doxycycline) administered through rodent bait stations can directly suppress the growth of *B. burgdorferi* in the mouse reservoir. A field study showed no *B. burgdorferi* infection in 102 small mammals administered doxycycline, and a 10-fold reduction in infection prevalence of questing nymphs.

CHALLENGES ON THE ROAD TO RODENT-TARGETED LYME PREVENTION

The global increase in Lyme disease burden and first studies on the effects of RTVs suggest that this approach could provide a solution for controlling disease on residential properties. But the move from traditional vaccines, designed to protect individual organisms, to vaccines that function in an environmental context also brings several challenges.

For one, RTVs are deployed in different ecological settings with various human and non-human populations. The behavior of these different populations and their interactions, socioeconomic factors and environmental concerns will play a considerable role in the success of these interventions. Mouse and tick populations can also vary from location to location and season to season; food bait could attract more than mice, or no mice at all.

There's also a cost component. Residents might find the commercial products too expensive, and while the collaboration within a neighborhood is likely to yield the best results, people might not work together or be able to afford to shield their communal areas. While [there are efforts](#) to implement Lyme disease interventions at community scale (e.g., surveillance, academic-public health collaborations, trials of control measures), most of them are still in pilot mode, or have been partially adopted. There is no systematic large-scale deployment of new tools like reservoir vaccines or mouse-targeted acaricides.

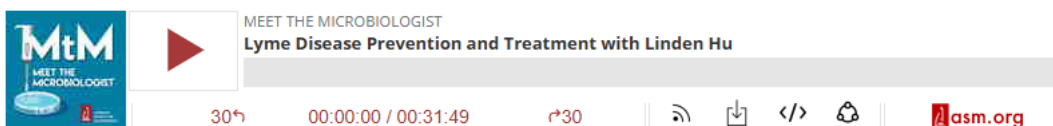
Environmental concerns play a role in evaluating the benefit of bait-based interventions, too. Field trials must prove safety for humans and other species in the affected area and demonstrate efficacy in different settings. The results are then subjected to regulatory requirements, which still vary across countries and need harmonization.

Watch: 'Can Sweat Prevent Lyme Disease?'

THE BOTTOM LINE

Despite the challenges, the growing global health burden of Lyme disease and the increasing cost for health systems propel the search for new solutions. New approaches in the pipeline—like targeting mice through specially designed baits—could shift Lyme disease prevention from reactive treatment to ecological control. Interventions that disrupt the enzootic cycle of Lyme disease plug into One Health frameworks integrating human, animal and ecosystem health, while underscoring the growing interest and need for public investment and international collaboration.

Learn more about research pertaining to the prevention, treatment and diagnosis of Lyme disease in this episode of *Meet the Microbiologist* featuring Linden Hu, M.D.



Click image to listen.