ADAPTIVE IMMUNITY

Care for the community

A memory-based immune system may have evolved in vertebrates because of the need to recognize and manage complex communities of beneficial microbes.

Margaret McFall-Ngai

All vertebrates have a type of immunity known as adaptive immunity, which allows them to respond to each fresh encounter with the microbial world on the basis of past interactions. Invertebrates, however, rely entirely on the innate immune system, an ancient mechanism present in all animals that does not typically 'remember' previous encounters. The remarkable memory component of the vertebrate adaptive system has been thought to provide heightened resistance to microbial pathogens. But this assumption presents a conundrum — invertebrates are no less challenged by the microbial world, nor are they less able to remain healthy.

How have invertebrates been so successful — they comprise more than 96% of animal species — without the benefit of an adaptive immune system? Many have thought the answer lies with lifestyle: because invertebrates are small, bear many young and are short-lived, they should have no need for a memory-based immune system that is suited to the long haul. But numerous invertebrates are large, have only a single offspring each year and live a long life. The quahog clam, for example, remains healthy for up to 250 years, despite pumping bacteria-rich sediments across its internal organs. Clearly, 'long-life' lifestyle features can evolve in the absence of an adaptive immune system. I propose a different explanation: that adaptive immunity has evolved in part to recognize and manage complex communities of beneficial microbes living on or in vertebrates.

Recent advances in molecular biology that allow biologists to quantify and identify an animal's normal microbiota suggest that the presence of complex communities of coevolved bacteria is a shared feature among vertebrates. In general, the coevolved partnerships of invertebrates seem to be much less diverse.

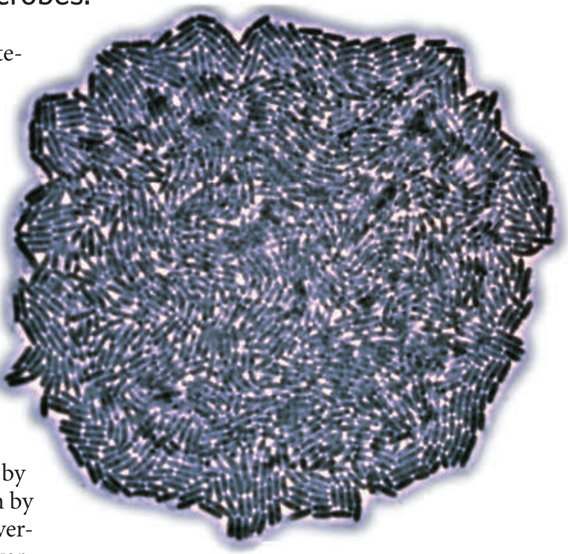
For example, characterization of human microbial partners has identified more than 2,000 bacterial species that typically associate as communities inside us — including on or in our skin, guts and mouth. These coevolved, resident communities are often in direct contact with our tissues, are relatively resistant to perturbations, such as starvation, and provide us with the metabolic benefit of millions of additional genes and activities. By contrast, fewer than 100 species of human bacterial pathogen have been identified, and exposure to these is generally rare and transient.

Meanwhile, evidence is emerging that most of the associations between invertebrates and the microbial world are different. Although an invertebrate gut tract can harbour dozens of bacterial species at any time, recent studies have identified only a small number (fewer than eight) of resident bacterial species. Thus, the gut microbiota of invertebrates is numerically dominated by tourists, with a composition dictated by the external environment rather than by stable residents, as is characteristic of vertebrates. Under these conditions, invertebrates might use their innate immune system to limit the range of interactions with the microbial world, treating all but a few species as unwelcome guests. By contrast, the evolution of the vertebrate immune system is likely to be strongly affected by the need to maintain a substantial resident microbiota.

The mechanisms by which invertebrates recognize and manage those resident microbial partners that they do have are unknown, but there are at least three possible strategies. First, there are examples in all major phyla of invertebrates that have beneficial bacterial associations with between one and three species that are maintained intracellularly, and so are invisible to the innate immune system. Although widespread among invertebrates, such associations seem to be absent from vertebrates.

A second strategy is to maintain a physical barrier between the host tissue and the microbes. The unusually complex, highly stable consortia harboured in the hindguts of termites and their relatives are effectively separated from the host tissues by a layer of chitin that precludes direct host–microbe interaction.

Third, even without a dedicated memory function, the innate immune system may be capable of managing the simple communities of resident bacteria typically present in the invertebrate gut. Recently, the number of specific recognition components of the innate system has been found to be much higher in some invertebrates than earlier estimates suggested; these specific recognition elements might provide a mechanism for keeping track of a number of microbial partners. The absence of these three strategies among vertebrates is consistent with the idea that the adaptive immune system has provided them with a different, more versatile microbial-management strategy.



Group effort: did microbial communities inspire the need for adaptive immunity?

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The advances in technology that have inspired these ideas should also allow us to test their predictions. Careful characterization of the gut microbiota of various vertebrates and invertebrates could address the basic premise that all vertebrates have a coevolved microbiota, whereas invertebrates rarely do. Similarly, comparative physiology could test the prediction that maintenance by vertebrates of coevolved microbial consortia, both throughout life and across generations, provides advantages, such as more efficient digestion, that are not available to invertebrates. Finally, there is the question of whether there is a price to be paid for the permissiveness of the adaptive immune system. Is autoimmunity a collateral consequence of the bargain we've cut with microbes? ■

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FURTHER READING

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