Preface

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It would seem inconceivable to anyone studying classical immunology that life could survive without the assistance of antibodies and lymphocytes. But most living things lack them. What is remarkable is that until the late 1970s, there was basically no discussion of how animals such as insects managed to coexist with microbes. Boman’s seminal discovery of cecropins changed the picture. Short cationic amphipathic peptides with antimicrobial activity, ‘antimicrobial peptides’ (AMPs) were discovered that could target the membranes of microbes but spared those of the host. As studies were extended into other organisms, including vertebrates, it became clear that AMPs were widespread throughout nature. Studies in Drosophila uncovered the intracellular circuits that controlled the expression of AMPs and analogous circuits were found to be conserved in vertebrates. We realized that vertebrates had simply added the equipment of adaptive immunity onto the ‘ancient’ immune equipment similar to this of the insects. Surprisingly, in states of health, the innate system, a non-inflammatory, clinically silent arm of immunity, does much of the hard lifting. For those of us interested in human innate immunity, the study of the insect provided clues to recognize the comparable vertebrate immune system. AMPs permit us to live in harmony with microbes.

We initially isolated AMPs on the basis of their antibiotic activity, essentially as we had conventional antibiotics. AMPs were clearly designed to kill microbes rapidly should these invaders enter spaces within a body that were intended to be sterile. By virtue of their mechanism of action, AMPs could keep resistant organisms at bay, attacking membrane targets that were too complex to modify through simple mutation. Multicellular organisms never depended on one AMP for defence, but rather a ‘cocktail’ of molecules that exhibited different antimicrobial spectra, and occasionally exhibited synergy. Some of these AMPs were produced constitutively, others after injury or microbial inoculation. The usual phylogenetic relationships between evolutionary distance and sequence similarity did not hold, in that each animal species seemed to have a unique array of AMPs with respect to both primary sequence and antimicrobial spectrum. A diverse array of receptors were subsequently discovered that recognized various microbial components, providing tissues and cells most likely to come into initial contact with microbes with the capacity to ‘taste’ the microbe, be it a bacterial, fungal or viral invader. In most cases, this information was found to be hardwired to a highly evolved effector arm, resulting in an orchestrated induction of AMPs and proteins. Depending on the context, the AMPs were discovered to be secreted from the endangered epithelium, expressed within the phagocytes attracted to the site of injury, or introduced into the circulation by an immune organ, such as the fat body in Drosophila. Indeed, it is fair to say that a ‘pathogen’ is a microbe that can overpower the defences presented by AMPs.

In this issue, Jens Rolff and Paul Schmid-Hempel have assembled a group of scientists who have made major contributions to our understanding of AMPs in the setting of the biology of invertebrates. They answer some of the most fascinating questions that come to mind in the field of innate immunity:

— What is behind the extraordinary diversity of AMPs?
— Why is resistance to AMPs within the biological context of an animal so unlikely to occur?
— How can animals constrain the growth of microbes that inhabit the ‘internal milieu’, and what role do AMPs play in this relationship?
— What are the immune defences of some lesser studied invertebrates such as nematodes and marine arthropods?
— How were AMPs discovered in the first place? For those who enjoy the history of a field, you can read a wonderfully personal account by a scientist who worked hand in hand with the pioneer.

If I might add one further question: One of the oldest known living animals is the Ming clam, found off the coast of Iceland in 2006, believed to be between 400 and 500 years old. What system of immunity can you conjure that could protect an animal for that period of time?