



## Objective Lens: Insect antimicrobial peptides as a promising source for antibiotic “substitutes”

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Currently, at least 2.8 million infections and over 700,000 deaths are reported from AMR bacterial infections globally (1,2). If no new antibiotics are isolated and made available by 2050, the CDC estimates that 10 million annual deaths will occur globally as a result of this inaction (5,8). Yet, surprisingly few have even heard of antibiotic-resistant bacteria, or understand the implications for global health. In fact, no new classes of antibiotics have been developed to treat microbial infections in well over 30 years, as pharmaceutical companies have instead pursued research and development of more lucrative drugs for non-infectious diseases. Since this trend is likely to continue into the foreseeable future, this crisis must be addressed using alternative creative approaches. Unfortunately, this problem is exacerbated poor antibiotic stewardship practices by healthcare providers and consumers for decades. The World Health Organization (WHO) has declared multidrug-resistant (MDR) bacterial and fungal pathogens to be one of the principal threats to global public health (5,7-9).

Alexander Fleming’s discovery of penicillin in 1928 was met with his own prediction that bacterial resistance to this “miracle drug” would soon be documented (3,4). In the 70+ years since

penicillin was introduced, overuse and misuse of antibiotics have contributed to the problem of MDR bacterial infections, as has the widespread use of antibiotics in agriculture for prophylaxis and growth promotion (8). In fact, the CDC has reported that over 70% of antibiotics used in the U.S. are in production animal environments (8-10). Clinically, antibiotic stewardship and surveillance programs have shown limited success in addressing the MDR crisis (9). In recent years, both the CDC and the White House have outlined clear goals and objectives for directly addressing antibiotic resistance in order to slow the spread of MDR bacteria, while offering a timeline on collaborative international efforts required to make this happen by 2020 (5,6). Unfortunately, this Executive Order signed by President Barack Obama (#13676) has not been addressed, during which time MDR bacterial infections have worsened and become more frequently diagnosed (6).

The global crisis of antimicrobial resistance (AMR) is fueled by antibiotic overuse in agriculture and human clinical applications. ESKAPE pathogens, identified by the World Health Organization as a priority for new antimicrobial drugs (11), are central to this pending catastrophe. However, it may be prudent to open a new line

of investigation in earnest evaluating insects as a largely unexplored source for novel antimicrobial peptides (AMPs), which show tremendous promise as an alternative for the use of antibiotics.

With over one million described species, insects are the largest class of organisms on the planet, and thus represent tremendous untapped potential for describing novel antimicrobial compounds (12). Insects adapt in remarkable ways to constant changes in their environments, including to a wide range of pathogens. This adaptability is due in large part to their immune systems, which respond quickly to invading microorganisms that gain entry into the hemocoel. A variety of AMPs comprise the key elements of an insect's humoral immune response; some of these molecules are involved in binding to bacterial cells, and facilitating their inactivation or elimination in unique ways. For example, many insect AMPs are positively charged and are thus attracted to the negative charge of bacterial surfaces, where they

may serve as membrane antagonists (disrupting bacterial cell structure), or are involved in a hemolymph coagulation response that prevents the bacterial pathogen from disseminating or growing within the insect host.

Insect AMPs are not only antibacterial, but have also been shown to have potential against fungal pathogens, some viruses, and cancer cell lines as well (12), although few if any of these molecules have been investigated more deeply with regard to their biotherapeutic practicality. Because these AMPs are unique in their mechanisms of action against target pathogens, little if any resistance issues have been observed, in stark contrast to traditional antibiotics (13), and this trait is arguably one of the most compelling reasons to investigate AMPs further as a promising means of treating the growing roster of drug-resistant bacterial pathogens. **This issue's cover features an artist's conceptualization of various insect AMPs.**

## References

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