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Discovery of novel bacterial toxins by genomics and computational biology

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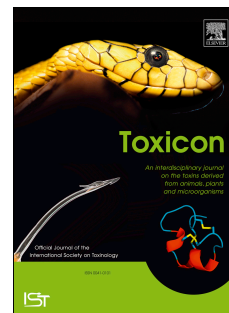
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1 **Discovery of novel bacterial toxins by genomics and computational biology**

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8 **Abstract**

9 Hundreds and hundreds of bacterial protein toxins are presently known. Traditionally, toxin
10 identification begins with pathological studies of bacterial infectious disease. Following
11 identification and cultivation of a bacterial pathogen, the protein toxin is purified from the
12 culture medium and its pathogenic activity is studied using the methods of biochemistry and
13 structural biology, cell biology, tissue and organ biology, and appropriate animal models,
14 supplemented by bioimaging techniques. The ongoing and explosive development of high-
15 throughput DNA sequencing and bioinformatic approaches have set in motion a revolution in
16 many fields of biology, including microbiology. One consequence is that genes encoding novel
17 bacterial toxins can be identified by bioinformatic and computational methods based on
18 previous knowledge accumulated from studies of the biology and pathology of thousands of
19 known bacterial protein toxins. Starting from the paradigmatic cases of diphtheria toxin,
20 tetanus and botulinum neurotoxins, this review discusses traditional experimental approaches
21 as well as bioinformatics and genomics-driven approaches that facilitate the discovery of novel
22 bacterial toxins. We discuss recent work on the identification of novel botulinum-like toxins
23 from genera such as *Weissella*, *Chryseobacterium*, and *Enterococcus*, and the implications of
24 these computationally identified toxins in the field. Finally, we discuss the promise of
25 metagenomics in the discovery of novel toxins and their ecological niches, and present data
26 suggesting the existence of uncharacterized, botulinum-like toxin genes in insect gut
27 metagenomes.

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