

# Genomics of the *Bacillus cereus* group of organisms <sup>☆</sup>

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## Abstract

Members of the *Bacillus cereus* group of organisms include *Bacillus cereus*, *Bacillus anthracis* and *Bacillus thuringiensis*. Collectively, these organisms represent microbes of high economic, medical and biodefense importance. Given this significance, this group contains the highest number of closely related fully sequenced genomes, giving the unique opportunity for thorough comparative genomic analyses. Much of the disease and host specificity of members of this group can be attributed to their plasmids, which vary in size and number. Chromosomes exhibit a high level of synteny and protein similarity, with limited differences in gene content, questioning the speciation of the group members. Genomic data have spurred functional studies that combined microarrays and proteomics. Recent advances are reviewed in this article and highlight the advantages of genomic approaches to the study of this important group of bacteria.

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**Keywords:** *Bacillus cereus*; *Bacillus anthracis*; Genome; Plasmid

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## 1. Introduction – The *Bacillus cereus* group of organisms

The *Bacillus cereus* group of organisms contains *Bacillus thuringiensis*, *Bacillus anthracis* and *Bacillus cereus* (*sensu stricto*). This group of Gram-positive spore-formers forms a highly homogeneous subdivision of the genus *Bacillus*. Demonstration of their high genetic relatedness has contributed to the suggestion that *B. anthracis*, *B. cereus* and *B. thuringiensis* are members of a single species, *B. cereus sensu lato* [1–3]. Traditionally, these organisms have been differentiated based on their phenotypic characteristics, including pathogenic potential. *Bacillus mycoides*, *Bacillus pseudomycooides* and *Bacillus weihenstephanensis* are also members of the *B. cereus* group of organisms. However, as no genomic data are available, these species have not been included in this review.

### 1.1. *Bacillus thuringiensis*

*B. thuringiensis* has long been regarded as an insect pathogen alone. The insecticidal spectrum varies within the 82 different serotypes reported [4], and affects insects primarily from the orders *Lepidoptera*, *Diptera* and *Coleoptera*. There are also reports of *B. thuringiensis* isolates active against mosquitoes that are vectors for disease, such as malaria and yellow fever [5]. *B. thuringiensis* spore preparations have been successfully commercialized as biopesticides. The spores are associated with large crystal protein inclusions, which can make up to 25% of the dry weight of the spore preparations. The crystals are aggregates of a large protein (about 130–140 kDa) that is actually a protoxin. Upon ingestion by insect larvae, the protoxin crystals solubilize in the mid-gut, where it is cleaved by a gut protease to produce an active toxin ( $\delta$ -endotoxins) of about 60 kDa. The toxin binds to the mid-gut epithelial cells, creating pores in the cell membranes. As a result, the gut is rapidly immobilized and the epithelial cells lyse. The insect larva stops feeding and often dies from lethal septicemia [6]. Little is known about the ecology of *B. thuringiensis* and conflicting reports are reviewed by Jensen et al. [7]. The *B. thuringiensis* natural environment is thought to be the insect host intestinal system. Upon

death of the insect the bacterium is released into the soil where *B. thuringiensis* is a ubiquitous inhabitant. In this environment and under favorable nutrient condition the spores could germinate and grow. The Cry genes encode the crystal toxins and are usually located on large, transmissible plasmids. The presence of Cry protein crystals in the spore is speculated to give *B. thuringiensis* an advantage in the soil environment upon sporulation [7] over *B. cereus*, *B. thuringiensis* is phenotypically distinguished from *B. cereus* only by the formation of intracellular protein crystals during sporulation. Overall, genetic studies have shown that *B. cereus* and *B. thuringiensis* are essentially identical [8]. In addition, like *B. cereus*, *B. thuringiensis* could be considered an opportunistic pathogen in animals and human [9–11].

### 1.2. *Bacillus cereus*

*B. cereus* is ubiquitous in nature and an opportunistic pathogen, often associated with two forms of human food poisoning, characterized by either diarrhea and abdominal distress or nausea and vomiting. In healthy individuals but mostly in individuals with certain underlying conditions such as, immunocompromised patients, or patients recovering from surgery, *B. cereus* has been known to cause a variety of infections, including: endophthalmitis, bacteremia, septicemia, endocarditis, salpingitis, cutaneous infections, pneumonia and meningitis [12,13]. *B. cereus* is found as a contaminant in many food products, including dairy products. However, its primary ecological niche is the soil environment. It is also commonly found as part of the gut microflora of invertebrates, not only as spores but also as growing vegetative cells [14]. By definition, *B. cereus* is acrySTALLIFEROUS, but a *B. cereus* strain carrying a functional cry gene is considered as a *B. thuringiensis* strain [15]. No virulence factors specific to *B. cereus* have been identified, and proteins thought to be specific to *B. cereus* have recently been found in *B. thuringiensis* isolates [6].

### 1.3. *B. anthracis*

*B. anthracis* is the etiological agent of anthrax, an acute fatal disease found primarily among herbivores,

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