Mining the botulinum genome

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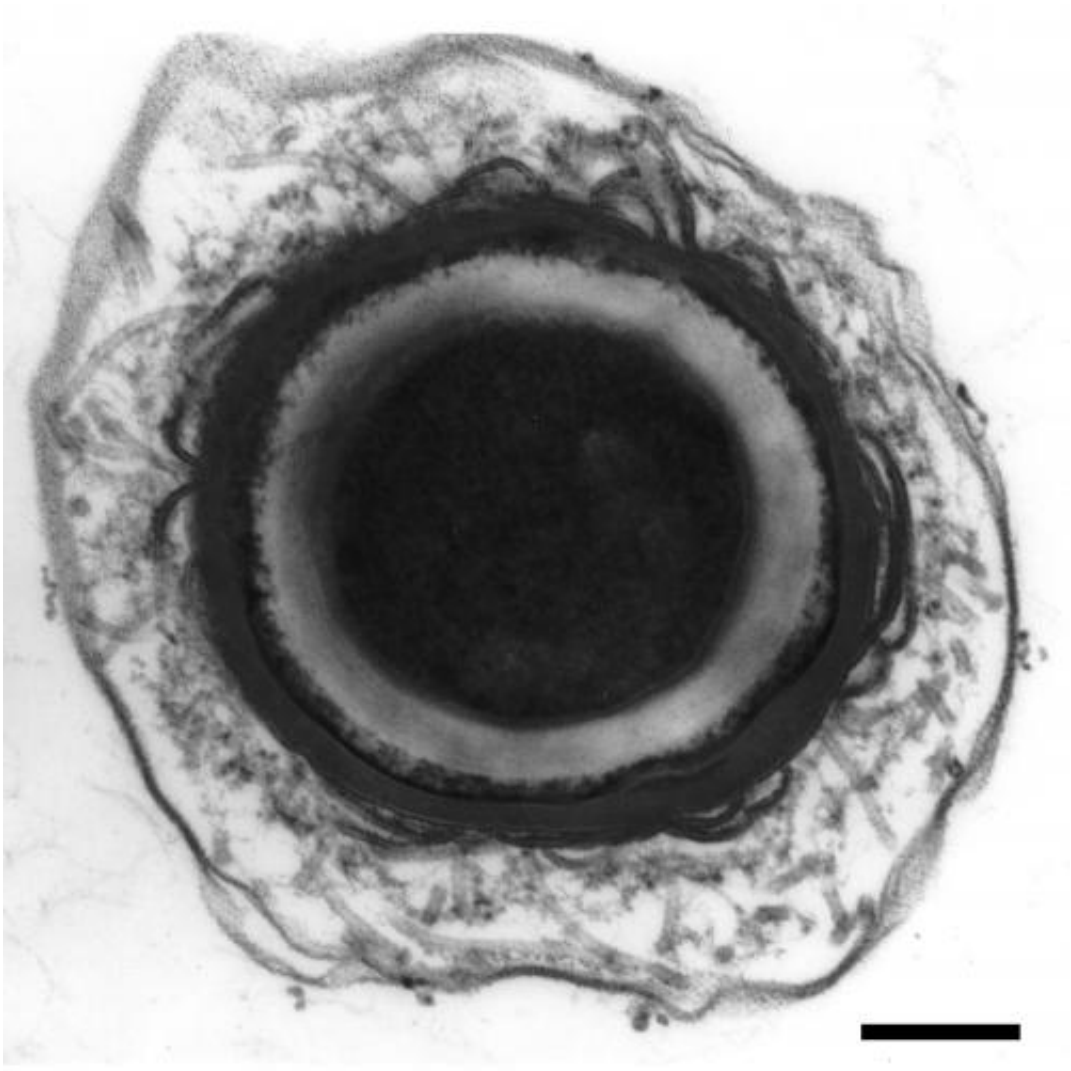


This is a spore of *Clostridium botulinum*. Credit: IFR

(Norwich BioScience Institutes) Scientists at the Institute of Food

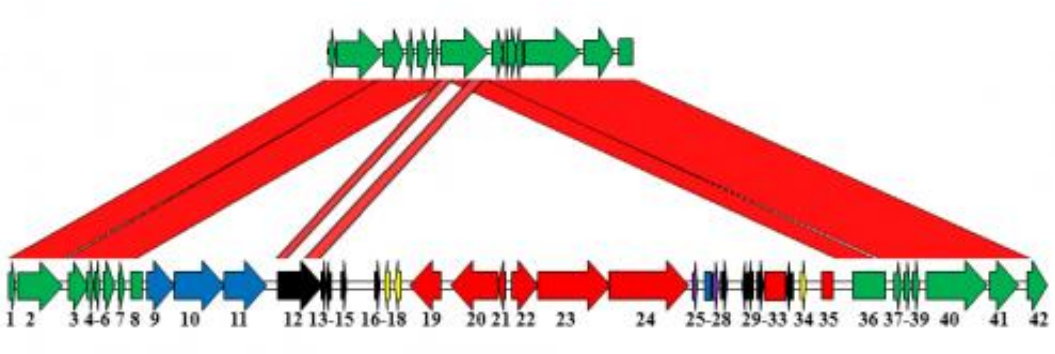
Research have been mining the genome of C. botulinum to uncover new information about the toxin genes that produce the potent toxin behind botulism.

The toxin that causes botulism is the most potent that we know of. Eating an amount of toxin just 1000th the weight of a grain of salt can be fatal, which is why so much effort has been put into keeping *Clostridium botulinum*, which produces the toxin, out of our food.

The Institute of Food Research on the Norwich Research Park has been part of that effort through studying the bacteria and the way they survive, multiply and cause such harm. In new research, IFR scientists have been mining the genome of *C. botulinum* to uncover new information about the toxin genes.

There are seven distinct, but similar, types of botulinum neurotoxin, produced by different strains of *C. botulinum* bacteria. Different sub-types of the neurotoxin appear to be associated with different strains of the bacteria. Genetic analysis of these genes will give us information about how they evolved.

Dr Andy Carter, working in Professor Mike Peck's research group, used data generated from sequencing efforts at The Genome Analysis Centre, on the Norwich Research Park. Andy compared the genome sequence of five different *C. botulinum* strains, all from the same group and all producing the same sub-type of neurotoxin.



Comparison of two closely related C. botulinum strains. Genes shared by both genomes are in green. The newly introduced DNA is shown by the gap in the red bars which connect the two DNA species. Genes in red are neurotoxin cluster associated including two extra ones, numbered 33 and 35, which are remnants of previous neurotoxin gene clusters that have been disrupted during the evolution of the current cluster. Gene number 12 (in black) is the new copy of the DNA replication gene.

An initial finding was that the five strains were remarkably similar in the area of the genome containing the neurotoxin gene. This suggests that the bacteria picked up the gene cluster in a single event, sometime in the past. Bacteria commonly acquire genes, or gene clusters, from other bacteria through this horizontal gene transfer. It is a way that bacteria have evolved to share 'weapons', such as antibiotic activity or the ability to produce toxins. To find out more about how *C. botulinum* acquired its own deadly weapon, Andy delved deeper into the genome sequence.

Like fossils of long lost organisms, Andy found, in the same region of the genome, evidence of two other genes for producing two of the other types of neurotoxin. Although these gene fragments are completely non-functional, finding them in the same place in the genome as the functional neurotoxin gene cluster is significant as it suggests that this region of the genome could be a 'hotspot' for gene transfer.

Looking to either side of the neurotoxin gene cluster uncovered more evidence supporting the hotspot idea. When the gene cluster inserted into the *C. botulinum* genome, it cut in two another gene. This gene is essential for the bacteria to replicate its DNA, so why does destroying it not prove fatal? *C. botulinum* was unaffected by this because contained in the segment of imported DNA was another version of the chopped-up gene.

Perhaps this is pointing us to the way *C. botulinum* first picks up its lethal weapon. This should help us prepare against the emergence of new strains, and may even one day help us disarm this deadly foe.

More information: The type F6 neurotoxin gene cluster locus of Group II Clostridium botulinum has evolved by successive disruption of two different ancestral precursors. Andrew T. Carter; Sandra C. Stringer; Martin D. Webb; Michael W. Peck. *Genome Biology and Evolution* 2013; doi: 10.1093/gbe/evt068

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