PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Flesh eater sequenced

ArticleInfo		
ArticleID	:	4333
ArticleDOI	:	10.1186/gb-2002-3-4-reports0022
ArticleCitationID	:	reports0022
ArticleSequenceNumber	:	23
ArticleCategory	:	Paper report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 2002–2–12 Received : 2002–2–12 OnlineDate : 2002–3–15
ArticleCopyright	:	BioMed Central Ltd2002
ArticleGrants	:	

ArticleContext	:	130593344

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Abstract

Analysis of the entire genome sequence of *Clostridium perfringens* will help explain how gas gangrene develops in humans

Significance and context

Clostridium perfringens is a Gram-positive anaerobic spore-forming bacterium found in soil, the intestines of humans and animals, and sewage. At temperatures between 10 and 60°C in anaerobic conditions and high moisture levels, toxins may be produced, and meat of any kind can be contaminated with spores. *C. perfringens* strains are classified into five groups (A-E) depending on their production of different toxins. The type A strain causes gas gangrene, necrotic enteritis, and mild diarrhea in humans. *C. perfringens*-induced diseases are among the most commonly reported food-borne illnesses.

After entry of vegetative cells or spores into the tissues, through a wound for example, rapid growth is observed, and toxins and degradative enzymes are produced, resulting in massive invasion and destruction of the tissues. Although toxin production and its regulation have been well studied, the pathogenesis and physiology of *C. perfringens* are not yet completely understood. A study of the entire genome sequence of *C. perfringens* reveals new insights in understanding the onset of the disease, and may contribute to the development of therapeutics to block *C. perfringens* invasion in humans.

Key results

Shimizu *et al*. determined the genome sequence of *C. perfringens* strain 13, classified as a type A strain. The genome contains 3,031,430 bp, has a remarkably low G+C content of 28.6% and contains 2,660 putative open reading frames (ORFs). A plasmid named pCP13 was also present and consists of 54,310 bp with a G+C content of 25.5% and 63 putative ORFs. Of the ORFs present in the genome, 56.1% showed similarity to functional genes in databases, 18.9% showed similarity to genes encoding unknown proteins, and 25.2% are unique to the *C. perfringens* genome. Comparison of the *C. perfringens* genome with the genome of the non-pathogenic *C. acetobutylicum* revealed interesting differences that may be related to their different lifestyles.For instance, genes encoding β- and α-galactosidases, β-mannosidase, and various virulence-associated proteins in *C. perfringens*were not found in *C. acetobutylicum*, whereas the latter contained genes encoding, for example, chemotaxis/

flagella-related proteins, and nitrogen-fixation genes that were absent from *C. perfringens*. *C. perfringens* can metabolize a variety of carbohydrate sources, including fructose, mannose, galactose, glycogen, lactose, and starch, which is consistent with the presence of many genes for carbohydrate-degrading enzymes - for instance, sucrase, β-mannosidase, and β-amylase. The genome includes 211 genes encoding putative transport systems involved in import or export of amino acids, cations/anions, carbohydrates, and nucleosides/nucleotides. Many genes related to spore formation or germination were found, but over 80 *Bacillus subtilis* genes involved in spore formation had no homologs in *C. perfringens*, suggesting a different mechanism of spore formation. All genes encoding toxins - for instance, hemolysin, phospholipase C, collagenase, enterotoxin, hyaluronidase, sialidase, and perfringolysin O - were found on the chromosome, with the exception of two that were found on the plasmid. Surprisingly, none of these virulence-related genes was present in pathogenicity islands - distinct regions of the genome present in some pathogens in which virulence genes are clustered together. Furthermore, 48 genes encoding bacterial two-component systems were found. One of these is the VirR/VirS system, which is involved in regulating the production of certain toxins.

Links

The genome sequence of *C. acetobutylicum* is available at the TIGR Microbial Database.

Conclusions

From the genome sequence, Shimizu *et al*. propose how *C. perfringens* could start its pathogenic life in human tissues. Shortly after invasion of human tissue through a wound, a suitable anaerobic environment is formed, causing rapid bacterial growth, degradation of carbohydrates and other host materials, and the generation of gas as a result of sugar fermentation, followed by the production of toxins, tissue destruction and deeper invasion. Shimizu *et al*. conclude that pathogenicity and utilization of nutrients must be tightly coupled in *C. perfringens* infection, and its nutritional features would be a possible target for inhibition of growth and prevention of infection.

Reporter's comments

After the determination of the genome sequence of *C. perfringens*by Shimizu *et al.*, the next step required to analyze this bacterium's pathogenicity will be to construct a set of (multiple) mutants to test the involvement of particular genes in the survival of *C. perfringens* within its host and in deeper infection. This will pave the way to the development of drugs that inhibit, for example, the function of different transport systems in the import of sugars or other nutritional material of host origin or the export of toxins, or that block the regulatory systems required for the production of the different toxins.

Table of links

Proceedings of the National Academy of Sciences of the United States of America

TIGR Microbial Database

References

1. Shimizu T, Ohtani K, Hirakawa H, Ohshima K, Yamashita A, Shiba T, Ogasawara N, Hattori M, Kuhara S, Hayashi H: Complete genome sequence of *Clostridium perfringens*, an anaerobic flesh-eater. Proc Natl Acad Sci USA. 2002, 99: 996-1001. 0027-8424