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

Three-way regulation of cholera toxin production

ArticleInfo		
ArticleID	:	4304
ArticleDOI	:	10.1186/gb-2002-3-10-reports0056
ArticleCitationID	:	reports0056
ArticleSequenceNumber	:	23
ArticleCategory	:	Paper report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2002–8–27 Received : 2002–8–27 OnlineDate : 2002–9–30
ArticleCopyright	:	Bio Med Central Ltd2002
ArticleGrants	:	

ArticleContext	:	13059331010

Wim D'Haeze

Summary

A three-component regulatory system involved in cholera toxin production has been characterized

Significance and context

Cholera is an acute diarrheal disease caused by infection of the intestine with the Gram-negative bacterium *Vibrio cholerae*. Infection can occur through drinking water or eating undercooked food contaminated with *V. cholerae*. Although the disease is rare nowadays in industrialized countries, it is still common, for example, in the Indian subcontinent and sub-Saharan Africa. Infection by *V. cholerae* to cause cholera requires both the production of toxin-coregulated pilus protein (TCP) and the cholera toxin (CT). The production of both is controlled by a complex cascade of regulators. A three-component VieSAB signal transduction system has previously been suspected of being involved in the regulation of toxin production. In contrast to conventional two-component systems, the VieSAB regulatory system contains two putative response regulators, VieA and VieB, as well as the sensor histidine kinase VieS. The *vieA* gene is expressed *in vitro*, in contrast to *vieB* which is expressed only *in vivo*, and *vieA* is dependent on TCP-mediated infection. Tischler *et al*. now show that the VieSAB three-component system is required for the full expression of the *ctxAB* operon, which encodes the A and B subunits of cholera toxin, during both growth *in vitro* and infection *in vivo*.

Key results

Using a combination of various *V. cholerae* mutants affecting *vieSAB*, RNA protection assays of RNA from wild-type *V. cholerae*, and the infant mouse model of cholera for *in vivo* studies, the authors show that the VieSAB system is not absolutely required for initial induction of *ctxA* and *ctxB in vivo* or *in vitro*, nor to reach the highest level of expression, but is needed to maintain *ctxAB* expression *in vitro*. Decreased production of ToxT, a positive regulator of *ctxA*, may explain the lowered expression of *ctxAB* in a *vieSAB V. cholerae* mutant. Western blot analyses showed that the decreased *ctxAB* expression in the absence of VieSAB correlated with a decrease in CT production. Finally, the affected *ctxAB* expression and CT production noted in a *vieSAB* mutant could be rescued by the introduction of the *vieSAB* genes *in trans*, upon introduction of a *vieSAB*-containing plasmid.

Links

The entire genome sequence of *V. cholerae* is accessible at The Institute of Genomic Research.

Reporter's comments

This study adds to our understanding of how genes required for cholera toxin production are regulated. Future research should include the identification of the environmental signals of human origin that are sensed by the VieSAB three-component system, the characterization of other *V. cholerae* genes that are putatively regulated by the VieSAB system, and the isolation of genes encoding other regulatory mechanisms that control toxin production.

Table of links

Journal of Bacteriology

The Institute for Genomic Research

References

1. Tischler AD, Lee SH, Camilli A: The *Vibrio cholerae vieSAB* locus encodes a pathway contributing to cholera toxin production. J Bacteriol. 2002, 184: 4104-4113.