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Abstract

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PI Title:	SCIENTIST
Project Title:	MOLECULAR BIOLOGY AND VIRULENCE OF CTX PHAGE

Abstract: DESCRIPTION (Adapted from the applicant's abstract): Cholera toxin is the principal virulence factor of Vibrio cholerae, the Gram-negative bacterium that causes the severe diarrheal disease cholera. The investigators recently discovered that this potent enterotoxin is encoded by a novel filamentous bacteriophage designated CTX. The CTX phage is the first filamentous phage known to result in the lysogenic conversion of a host bacterium. The CTX phage can integrate into the V. cholerae chromosome and form stable lysogens or, after induction, excise from the chromosome and replicate as a plasmid. During this replicative stage of the phage life-cycle, cholera toxin can be expressed independently of the factors which were believed to be essential for its expression. Our demonstration of the induction of CTX phage from V. cholerae lysogens within the host gastrointestinal tract suggests the possibility that in vivo CTX phage induction plays a significant role in the virulence of V. cholerae. The objectives of the proposed studies are to understand the life-cycle of the CTX phage at the molecular level and to assess the significance of this bacteriophage in the pathogenesis of cholera. These studies will establish the molecular biology of a mechanism of horizontal transfer of virulence genes and thereby further our understanding of the emergence of pathogens. The study of the intraintestinal induction of CTX phage from lysogens, could establish a new paradigm for understanding the regulation of the expression of phage encoded virulence factors in a variety of bacterial pathogens that are lysogenized with converting phage. This work will also have important ramifications for the design of safer live attenuated V. cholerae vaccine strains.

Thesaurus Terms:
bacterial virus, cholera toxin, life cycle, lysogeny, molecular biology, virulence, virus genetics
Vibrio cholerae, bacteriophage M13, cholera, gene expression, gene induction /repression laboratory mouse, polymerase chain reaction, protein purification

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