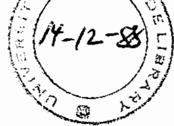

Haemagglutinins of *Vibrio cholerae*: Molecular Characterization of the Mannose-Fucose Resistant Haemagglutinin (MFRHA).

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Abstract

The disease cholera is caused by *V. cholerae* of the O1 serotype. In contrast to organisms such as *Shigella* and *Salmonella*, *V. cholerae* is a non-invasive pathogen. It has been recognized that one of the most essential steps in the onset of cholera is the colonization of the small intestine. Hence considerable interest has been shown in identifying which factors may act as adhesins in the attachment of these organisms. Since 1961, when Bales and Lankford suggested that interaction between *V. cholerae* and red blood cells mimics that of the organism with the intestinal epithelium, a number of workers have become interested in the various haemagglutinins of *V. cholerae* and their properties. Hanne and Finkelstein (1982) have described four distinct haemagglutinins. One of these haemagglutinins is termed the mannose-fucose resistant haemagglutinin (MFRHA) and is found in all *V. cholerae* strains regardless of biotype. The general aim of this thesis is to report the first cloning, sequencing and detailed analysis of a gene encoding one of the *V. cholerae* haemagglutinins and to give some indication of whether the MFRHA protein may play a role in pathogenesis.

Chapter 3 describes the cloning and isolation of the MFRHA gene, characterization of its properties, localization of the coding region to within a 0.72 kb region and identification of the protein products using minicell analysis. The MFRHA gene was isolated from both biotypes and was shown to be identical. Chapter 4 analyzes the genetic organization of the MFRHA gene. This included sequencing of a 1,398 bp segment of *V. cholerae* DNA. Chapter 5 describes the construction of a deletion mutation in the MFRHA gene followed by insertion of an antibiotic marker and introduction of such a mutation into the *V .cholerae* chromosome.

Research of other Gram-negative pathogens suggests haemagglutinins are likely candidates for adhesins. Due to the number of *V. cholerae* haemagglutinins and the lack of characterization, one can only analyze their contribution by cloning the genes and introduction of specific mutations into the chromosome.

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