

TITLE

Understanding the Functions and Implications of FadR in *Vibrio cholerae*

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ABSTRACT

Cholera is a bacterial disease caused by ingestion of the bacterium *Vibrio cholerae* through contaminated food or water. The main symptom of cholera is diarrhea, which leads to approximately 142,000 deaths from fatal dehydration annually. The transcription factor, FadR, is the master regulator of fatty acid metabolism and plays a key role in *V. cholerae* virulence. The level of fatty acids inside the bacterium regulate the production of cholera toxicity factors and also influences the activity of FadR. Using X-ray crystallography, the structure of FadR was solved in both the presence and absence of DNA and the fatty acid ligand, oleoyl-CoA. In the absence of a ligand, the FadR dimer adopts a conformation capable of binding DNA. In the ligand bound structure of *V. cholerae* FadR, two fatty acid binding sites were identified. The second fatty acid binding site was discovered to be made up of a 40 amino acid insertion in the protein that is absent in *E. coli* FadR. In the presence of a second ligand, FadR undergoes a dramatic conformational change causing the protein to release from DNA. The additional fatty acid binding site in the *V. cholerae* version of FadR may improve transcriptional regulation and efficiency compared to its *E. coli* counterpart.