

The cAMP receptor protein controls *Vibrio cholerae* gene expression in response to host colonisation

Jainaba Roussel

jaimanneh@yahoo.co.uk

Home: MRCG at the LSHTM, Fajara, The Gambia

Study: University of Birmingham, Edgbaston, B15 2TT

The bacterium *Vibrio cholerae* is the causative agent of the acute diarrhoeal disease cholera. *V. cholerae* is naturally found in aquatic environments but can switch lifestyles to cause disease in humans. The lifestyle switch requires modulation of genetic systems. Much of the regulation occurs at the level of gene expression and is controlled by transcription factors. In this work, I show that the global transcription regulator, cAMP receptor protein (CRP), plays an integral role in the regulatory network that controls lifestyle switching. I have identified two sites for CRP in the intergenic region between *rtxHCA* and *rtxBDE*, a locus which encodes the multifunctional-autoprocessing repeats-in-toxin (MARTX) toxin and toxin transport system respectively. Using a combination of genetics, biochemistry and *in vivo* animal studies, I have determined a CRP dependent regulation of gene expression for toxin transport in response to host infection. This work shows that *rtxHCA* is constitutively expressed and not subject to regulation by CRP whilst CRP acts as a repressor of *rtxBDE* transcription. Examination of further CRP targeted genes reveals similar behaviour upon host colonisation. These findings suggest that toxin export occurs in nutritionally rich environments, where the MARTX toxin can exert cytopathic and cytotoxic effects on host cells.