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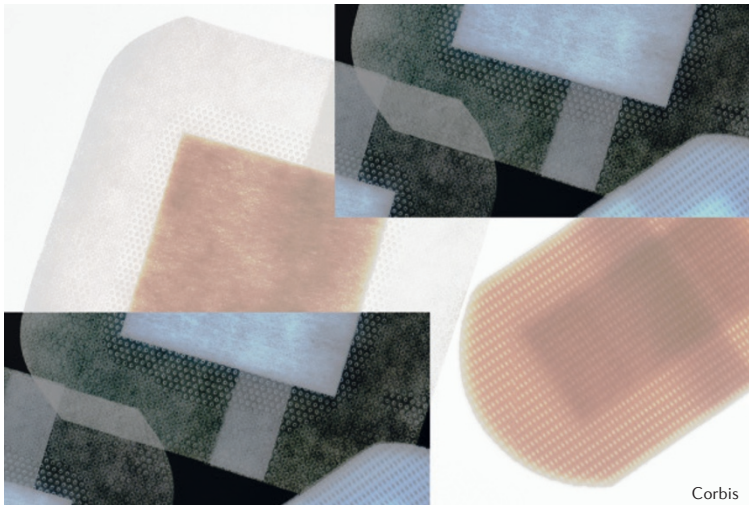
BACTERIAL PATHOGENESIS

# First aid kit for cholera

> *R. obeum* restricted pathogen colonization and reduced the expression of *V. cholerae* virulence factors



Corbis

Invasion of the human small intestine by the enteropathogen *Vibrio cholerae* leads to acute diarrhoeal disease. In a new study, Gordon and colleagues examined the role of the human gut microbiota in *V. cholerae* infection and showed that one of its members, *Ruminococcus obeum*, decreases the expression of *V. cholerae* virulence factors to limit colonization.

The authors used a metagenomics approach to analyse the bacterial composition of faecal samples collected from seven infected Bangladeshi adults and healthy controls. They showed that during the early phases of diarrhoea, the microbiota was divergent from the healthy adult microbiota, with *V. cholerae* as well as *Streptococcus* and *Fusobacterium* species being dominant, while during recovery, a healthy microbial community, including *Bacteriodes*, *Ruminococcus* and *Prevotella* species, was restored. Interestingly, several bacterial species that have previously been shown to be associated with the assembly and maturation of the gut microbiota in healthy Bangladeshi children were present in samples collected during the recovery phase. This suggests that similar processes underlie normal postnatal community assembly and microbiota restoration after disruption.

To determine if these recovery-associated species have a role in limiting *V. cholerae* infection, the authors colonized gnotobiotic mice with an artificial community composed of 14 human gut bacterial species that correlated with recovery from cholera in adults and with normal microbiota maturation in children. Following infection, the levels of *V. cholerae* in mice with the artificial human gut microbiota were lower compared with control gnotobiotic mice. In addition, the authors found that the abundance of one of the members of the artificial microbiota, *R. obeum*, was consistently increased following infection and, using mono- and co-colonization experiments, they showed that *R. obeum* restricted pathogen colonization and reduced the expression of *V. cholerae* virulence factors.

So, how does *R. obeum* limit *V. cholerae* colonization? Expression of *V. cholerae* virulence factors is repressed by an interspecies quorum sensing pathway that involves the signalling molecule autoinducer 2 (AI-2). Consistent with this, the authors found that expression of *R. obeum* AI-2 and the AI-2 synthase LuxS were increased following *V. cholerae* invasion and that *R. obeum* AI-2 represses *V. cholerae* virulence factor expression. Finally, the authors demonstrated that *R. obeum*-mediated modulation of *V. cholerae* colonization does not depend on the *V. cholerae* AI-2 sensor LuxP or other downstream regulatory genes that have been implicated in *V. cholerae* virulence gene expression, which suggests that *R. obeum* regulates virulence through a novel pathway.

Future studies should identify other members of the human microbiota that use quorum sensing — or possibly other mechanisms — to limit enteropathogen infections.

*Andrea Du Toit*

**ORIGINAL RESEARCH PAPER** Hsiao, A. *et al.* Members of the human gut microbiota involved in recovery from *Vibrio cholerae* infection. *Nature* http://dx.doi.org/10.1038/nature13738 (2014)