The illustration shows the mirror image forms of L- and D-methionine with *Vibrio cholerae* and was based on an image provided by H. Lam, Brigham and Women's Hospital, Boston, USA.

BACTERIAL PHYSIOLOGY

Mirror signal, manoeuvre

A recent *Science* paper from the Waldor laboratory provides evidence that bacteria use D-amino acids to remodel the cell wall during the adaptation to stationary phase.

Almost all naturally occurring proteinogenic amino acids are chiral and, as such, can exist as L- and D-form mirror-image stereoisomers. In nature, L-forms predominate, and few biological functions have been assigned to D-amino acids. In bacteria, however, two D-amino acids, D-Ala and D-Glu, are incorporated into the cell wall peptidoglycan. Lam, Oh, Cava and colleagues were investigating cell wall synthesis in *Vibrio cholerae* when they noticed that *V. cholerae* cells with a mutation in one of the penicillin-binding proteins involved in peptidoglycan synthesis underwent an unusual morphological transition from rod-shaped to coccoid cells during stationary phase. This switch was controlled by a soluble factor or factors that are secreted into the culture supernatant. Fractionation of stationary-phase supernatants revealed the presence of D-amino acids, and a time course analysis showed that these amino acids accumulated in the supernatant to millimolar levels during stationary phase. D-Ala and D-Glu are known to be produced from their L-form enantiomers by an amino acid racemase. Lam *et al.* identified a gene encoding a periplasmic racemase in *V. cholerae*, *vc1312*, which they renamed *bsrV* (broad-spectrum racemase *Vibrio*). D-amino acid production in Δ*bsrV* cells was greatly reduced compared with production in wild-type cells.

As cells enter stationary phase they shut down unnecessary metabolic pathways. So why divert resources to the production of D-amino acids? The authors looked at the composition of the peptidoglycan in wild-type and Δ*bsrV V. cholerae* and found that, although there were no differences during exponential growth, Δ*bsrV* stationary-phase cells contained twice as much peptidoglycan as wild-type stationary-phase cells. There were also differences in peptidoglycan structure, and peptidoglycan from Δ*bsrV* cells was less resistant to osmotic stress than that from wild-type *V. cholerae* cells. The authors conclude that the production of D-amino acids by the BsrV racemase regulates the amount and composition of peptidoglycan in *V. cholerae* stationary-phase cells. The mechanisms involved remain to be fully determined, but high-performance liquid chromatography analysis revealed that D-Met could be incorporated into *V. cholerae* peptidoglycan. Further work suggested that D-amino acids might also regulate the activity of the penicillin-binding proteins that are responsible for peptidoglycan synthesis and modification.

Finally, Lam *et al.* showed that this phenomenon is not restricted to *V. cholerae*. The production of D-amino acids and the presence of putative racemases were observed in many other species, including *Bacillus subtilis* and *Staphylococcus aureus*. More detailed analysis of the effects of D-amino acid production on *B. subtilis* stationary-phase cultures showed that D-amino acids also downregulate peptidoglycan synthesis in this species.

These results suggest that bacteria use D-amino acids to regulate the cell wall remodelling that is required on entry to stationary phase, and the authors propose that D-amino acids could be used to synchronously control this process in a bacterial population. Further work is required to elucidate the details of the mechanisms involved, and this work shows that there is still much to be uncovered about the roles of D-amino acids in bacteria.

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ORIGINAL RESEARCH PAPER Lam, H. *et al.* D-Amino acids govern stationary phase cell wall remodelling in bacteria. *Science* **325**, 1552–1555 (2009)