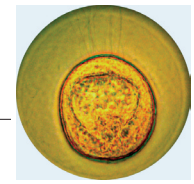
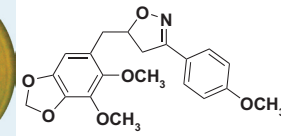
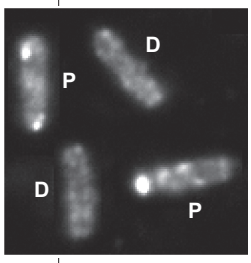
acs chemical biology

# In this ISSUE





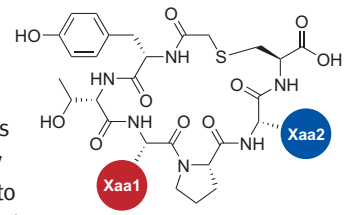

## Should I Stay or Should I Go?




Many bacteria can move toward stimuli that attract and away from those that repel. At the molecular level, responding signals are conveyed from the periplasm to the internal cytoplasm *via* a two-component phosphorelay system that requires methyl-accepting chemotaxis proteins (MCPs). In the gut bacterium, *Escherichia coli,* five types of MCPs sense dozens of different stimuli. Binding an attractant leads to the bacterium "running" toward the stimulus, while repellents cause it to "tumble" away from the source. Borrok and colleagues (p 101 and Point of View p 89) show that stimuli are perceived as attractants or repellents through changes in the cellular lattice of MCPs.

The authors synthesized a derivative of leucine and showed that it is an effective repellant. They then synthesized a ligand that presented multiple copies of this derivative. Astonishingly, this multivalent ligand functioned not as a repellant, but as an attractant. In both cases, stimuli were sensed through the same MCP. The authors demonstrate that high valency repellents actually act as attractants by disrupting the signaling lattice. These findings provide valuable insight into the mechanisms of bacterial chemotaxis and have intriguing implications for eukaryotic signal transduction.

## Peptides Close the Gap




Peptides with unusual bonds, including cyclic peptides, have been difficult to synthesize through ribosomal translation. Goto and colleagues (p 120 and Point of View p 87) describe a process for synthesizing cyclic peptides by combining a cell-free translation system with an artificially evolved ribozyme that attaches an amino acid of interest on to the initiator transfer RNA. The authors demonstrate the general applicability of this system in incorporating formylated versions of the 20 common amino acids at a programmed start codon. They also demonstrate that higher efficiencies for amino acids that are poorly incorporated can be obtained by adding a specific modification.

Extending this study further, the authors show that their system can incorporate a wide variety of derivatives with N-terminal modifications. This allows them to apply this unique strategy to synthesize a cyclic peptide with anticancer properties. As the authors point out, cyclization of the peptide proceeds spontaneously using this method. Applied broadly, this new technology should allow the assembly of cyclic peptides of various ring size.

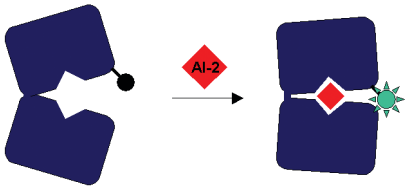
## A Farewell to Cilia

From a human perspective, the sea urchin might be thought of primarily as a source of culinary ingredients, but embryos of this echinoderm also serve a purpose in molecular, cellular, and developmental biology. The sea urchin embryo is used as a model system for determining the antiproliferative, antimitotic, and tubulin-stabilizing effects of chemical compounds.

Semenova and colleagues (p 95 and Point of View p 84) utilize rapidly developing sea urchin embryos to screen a series of small molecules for their effects on cell division and the timing of morphogenetic stages. They show that two derivatives have no observable effect other than to render the sea urchin embryos immotile. The authors demonstrate that this immobilization is reversible. One compound that the authors test is exquisitely selective; it causes the loss of only motile cilia but does not affect immotile sensory cilia. As a result of this study, a convenient tool now exists for understanding the various roles of cilia in developing organisms.

## Eavesdropping on Bacteria

Bacterial cells communicate with other cells of the same or different species by a process known as quorum sensing. In this process, the key small molecules that bacterial cells use to "talk" are known as autoinducers. One cell produces and releases these molecules, and another detects and acts in response. In many species, a number of processes associated with infection occur through this form of communication. Zhu and Pei (p 110) present a robust platform for the detection and quantitation of autoinducers involved in interspecies communication.




The authors design a sensitive set of biosensors by modifying autoinducer receptor proteins that "hear" at the receiving end of the quorum-sensing signaling chain. This assay is quantitative and can be used for real-time detection. The authors then use this assay to detect a particular autoinducer from various bacterial species. In the long run, being able to eavesdrop on bacterial communication will allow scientists to better understand many cellular processes associated with bacterial infections.

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