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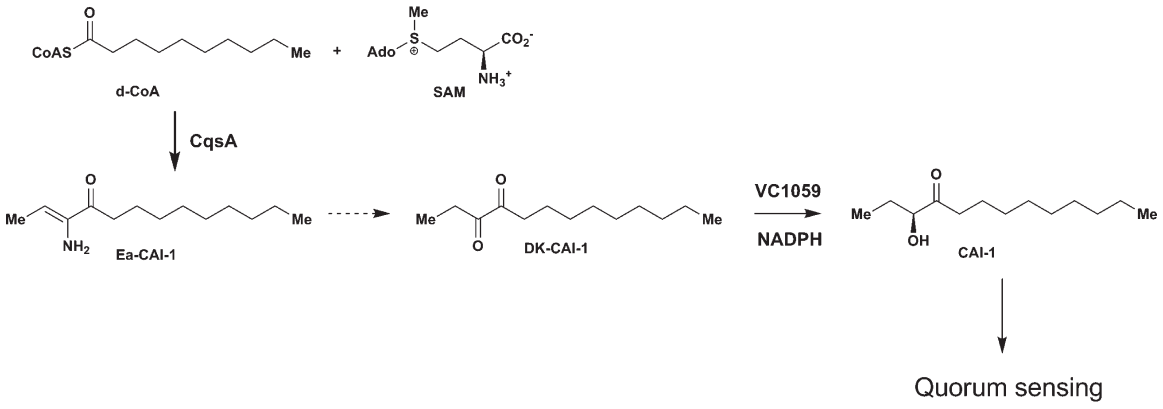
Biosynthesis of a Bacterial Communication Signal

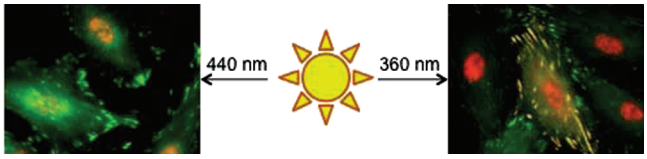
Bacteria can coordinate their gene expression by assessing their population density through cell-to-cell communication known as quorum sensing. Communication occurs via the production of freely diffusible signal molecules known as autoinducers. Extracellular concentrations of autoinducers increase with the proportional rise in bacterial cell density. Once autoinducer levels reach a threshold concentration, bacteria that sense these small molecules alter their gene expression patterns in a coordinated manner. Several pathogenic bacteria use quorum sensing as a means to control the production of virulence factors. In this issue, Wei *et al.* (DOI: 10.1021/cb1003652) describe the biosynthesis of a key signal molecule involved in virulence, CAI-1 in the human pathogen *Vibrio cholerae*.



Previous studies have identified CqsA as a key biosynthetic enzyme of autoinducer (*S*)-3-hydroxytridecan-4-one (CAI-1). However, the pathway for CAI-1 production remained elusive. In an elegant study, the authors provide substantial evidence for a three-step process in the biosynthesis of CAI-1. In a never before reported reaction, CsqA couples (*S*)-adenosylmethionine (SAM) with a second substrate, decanoyl-coenzymeA, producing the previously unidentified intermediate signaling molecule, 3-aminotridec-2-en-4-one. The unique mechanism of CsqA activity involves a single-step enzymatic PLP-dependent β,γ-elimination of SAM and an acyltransferase-catalyzed reaction. The second step is presumed to involve the spontaneous conversion of 3-aminotridec-2-en-4-one to tridecane-3,4-dione. A newly identified dehydrogenase, VC1059 was shown to be involved in the subsequent NADPH-dependent conversion of tridec-3,4-dione to CAI-1. Given the involvement of the CAI-1 signaling pathway in the life cycle and virulence of *V. cholerae*, the current study provides new targets for the development of therapeutics.

Selective Triggering of Distinct Protein Kinase Pathways by Light

Signaling pathways, such as those driven by protein kinases, control cellular phenotypes and are closely influenced by the spatiotemporal context in which they function. Spatiotemporal resolution studies of biological elements have often relied upon photoactivatable or "caged" compounds. Unfortunately, caged compounds are activated by UV light, which does not allow the independent control of more than one element associated with a signaling network at a time. To this end, Priestman *et al.* (DOI: 10.1021/cb100398e) describe a powerful combination of visible-absorbing and near-UV caged compounds to control independent protein kinase pathways.



cGMP- and cAMP-dependent protein kinases (PKG and PKA, respectively) are homologous enzymes that play a role in the phosphorylation of proteins. Apart from phosphorylating their own independent substrates, they are known to modify some common proteins. To distinguish between the cGMP- and cAMP-mediated pathways, the authors used nitrobenzyl-caged PKG and a coumarin-caged cAMP that are photoactivated at 360 and 440 nm respectively. The dual wavelength activation was evaluated by studying the phosphorylation of a substrate common between the two enzymes, vasodilator-stimulated phosphoprotein (VASP). Remarkably, PKA phosphorylates VASP at serine residue 157 upon exposure to light at 440 nm, whereas PKG modifies serine residues 157 and 239 at 360 nm. These new tools provide a platform for studying two closely related intracellular signaling pathways by phototriggering in a wavelength-specific manner.

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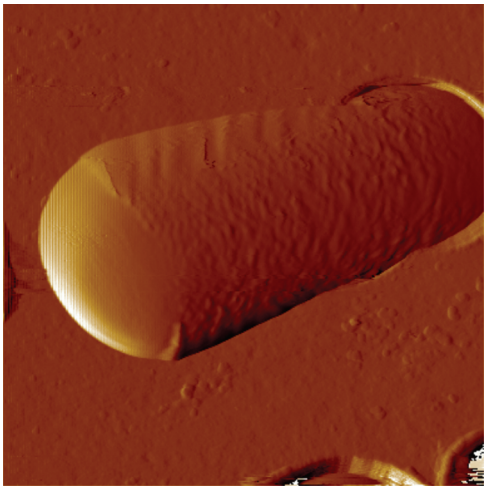
Teichoic Acids Shape Bacterial Cells

Up to 50% of the Gram-positive cell wall weight comprises teichoic acids (TAs). These complex polysaccharide anionic glycopolymers have been implicated in scavenging cations and creating a pH gradient across the cell wall. More importantly, TAs play a role in the morphogenesis of the bacterial cell and in cell elongation and division. Although much is known about the structure and biosynthesis of TAs, details of their spatial organization are poorly understood. Using a powerful combination of single-molecule atomic force microscopy (AFM) and fluorescence microscopy, Andre *et al.* (DOI: 10.1021/cb1003509) define the distribution of TAs in relation with their physiological roles.



The wall-teichoic acids (WTAs) of *Lactobacillus plantarum* are covalently linked to peptidoglycan. To study the subcellular localization and function of WTA, a mutant strain lacking the *tagO* gene that encodes a key WTA biosynthesis enzyme was constructed. The Δ*tagO* strain exhibited aberrations in cellular morphology, elongation, and division as compared with wild-type strains. Fluorescence imaging using a lectin probe (concanavalin A) and live cell imaging by AFM revealed that surface morphology of the cells is highly polar, with the sides exhibiting a rough morphology and the poles exhibiting a smooth morphology, and that the morphological characteristics correlate with the localization of WTA in the cell wall. Characterization of bacterial cell mutants using a combination fluorescence and nanoscale AFM imaging of live cells provides a robust platform for imaging the wall constituents in bacterial cells and offers a powerful avenue for studying structure−function relationships of teichoic acids in live cells.