Title: Shining a light on an opportunistic pathogen

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Abstract

The opportunistic pathogen *Acinetobacter baumannii* uses a BLUF-domain protein to respond to light, altering its motility behavior, biofilm formation, and perhaps its virulence.
Commentary

The surface of our planet is subjected to dramatic changes in levels of solar radiation on a daily basis. Sunlight is the direct energy source for photosynthetic organisms and is the foundation for most food chains that support heterotrophs like ourselves. Not surprisingly, plants and photosynthetic microorganisms sense and respond to light in many ways. Prokaryotic light sensors are diverse and include phytochromes, rhodopsins, blue-light-sensing using flavin (BLUF)-domain proteins, light oxygen and voltage sensing (LOV)-family proteins, and others (1, 6, 11). These photoreceptors regulate responses such as migration to regions with optimal wavelength and intensity of light, expression of genes involved in harvesting light energy, and expression of genes involved in protection from light mediated damage. Those of us who study non-phototrophic organisms often ignore light as a variable in our experimental designs. Although we are exquisitely sensitive to light, we expect our experimental subjects to be blind and indifferent to this rich source of information about their environment. However, several examples of light-induced behaviors have been reported recently in non-phototrophic prokaryotes, and analysis of genome sequences suggests that this may be a common phenomenon (6, 8, 10, 11). In this issue of Journal of Bacteriology Mussi et. al. describe the response of the important opportunistic pathogen *Acinetobacter baumannii* to blue light, and the identification of the photoreceptor involved in light sensing (5).

*A. baumannii* is a Gram-negative γ-proteobacterium and a common opportunistic pathogen (9). It is a hardy bacterium that survives well in a hospital setting, and many multi-drug resistant strains have arisen, limiting treatment options. Given the clinical
importance of *A. baumannii* surprisingly little is known regarding its mechanisms of pathogenicity, although recent studies have begun to identify potential virulence genes (7).

In spite of its name (derived from the Greek 'akineto' meaning motionless or nonmotile), and its lack of flagella, *A. baumannii* spreads rapidly over surfaces. This is likely the result of 'twitching motility', a form of surface translocation first described for members of the genus *Acinetobacter* (2, 3) and later identified in numerous other bacteria. Extension and retraction of Type IV pili are responsible for cell movement by twitching motility (4). Mussi et. al. made the unexpected discovery that exposure to light resulted in dramatic differences in motility behavior. Cells formed spreading colonies in the dark, but formed nonspreading colonies when incubated under blue light. Genome sequence analysis suggested a likely candidate for the photoreceptor involved in this process: a BLUF-domain containing protein referred to as BlsA (blue-light-sensing A). Disruption of *blsA* eliminated the inhibitory effect of blue light on motility, and spectral analysis of recombinant BlsA protein confirmed its responsiveness to blue light.

The responses mediated by BlsA are not limited to motility. Blue light also eliminated the formation of biofilms and pellicles in broth grown cultures, and blue light enhanced the ability of *A. baumannii* to kill cells of the eukaryotic fungus *Candida albicans*. Each of these effects also required BlsA. The ability to interact with and damage cells of *C. albicans* may have relevance to disease conditions caused by *A. baumannii*, since there may be common elements involved in *A. baumannii* mediated damage to *Candida albicans*, and to human cells and tissues.
The results presented raise many questions for future study. Clearly BlsA controls motility, but the mechanism is not known. Does blue light regulate expression of motility genes or the functioning of the motility machinery? What is the nature of the motility machinery? Type IV pili are the likely motility organelles due to the presence of key genes such as *pilT* in the genome, and the occurrence of pilus-associated twitching motility in other members of the genus (2), but this needs to be demonstrated. What proteins lie immediately downstream of BlsA and how is the signal generated by BlsA transduced to give rise to the observed phenotypes? The blue light effect disappears when cells are incubated at 37°C. Is decreased expression of *blsA* the mechanism for this temperature effect as suggested by the authors? Is there physiological significance to the temperature effect? Perhaps the cells have become blind to light at 37°C because there is no positive selection to respond to light in the relative darkness of the host tissues. How are *C. albicans* cells damaged by *A. baumannii*? Are similar mechanisms used to damage cells of a human host? How widespread is this phenomenon among members of the genus *Acinetobacter*? Many other members of the genus are common nonpathogenic environmental bacteria. Do they exhibit the light-mediated responses described for *A. baumannii*? Further experiments will be needed to determine whether the enhanced fungal killing in response to light translates to enhanced virulence in an animal or human host. Clearly the light mediated effects are not detected at the temperature of the human body. Nevertheless, sensing and responding to light may allow the pathogen to survive outside of the human body in hospital settings, and may prepare the pathogen for its next encounter with a susceptible host. An improved understanding of the *A. baumannii* response to light may suggest strategies to mitigate its virulence.
BLUF domain proteins and other photoreceptors are found in numerous heterotrophic prokaryotes (11). In the vast majority of cases the functions for these photoreceptors are not known. Perhaps the results of Mussi et al. will encourage other microbiologists to open their incubators and let the sun shine in. The results may be illuminating.


