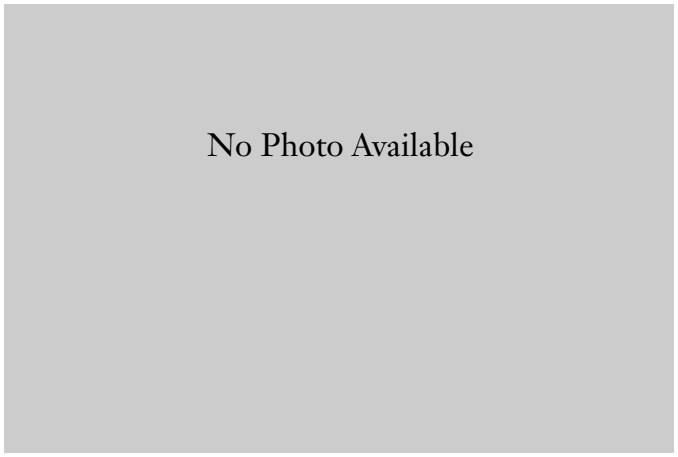
EXPLORE THE ISSUE BEING INVESTIGATED

How *Pseudomonas* "Sugar-coats" Itself to Cause Chronic Lung Infection



Viewed from a bacterium's point of view, infection is a chancy proposition at best. For a bacterial colony to establish itself, there must be a rich supply of nutrients, ample moisture that's not too salty, and a temperature that does not get too high. Starvation, dessication from lack of water or osmotic loss of water due to high salt, and retardation of growth by high temperature are all dangerous environmental risks to a bacterium like *Pseudomonas aeruginosa* trying to establish itself in a human lung.

That is why P*seudomonas s*ucceeds so rarely in infecting people's lungs. The exceptions are cystic fibrosis patients. *Pseudomonas* often succeeds in forming chronic colonies in the respiratory tracts of cystic fibrosis patients. Because of the very salty conditions encountered there, few bacteria would be expected to thrive. *Pseudomonas*, however, has evolved a mechanism that protects it against this sort of stress. It sugar-coats itself.

What at first seems silly is in actuality a clever strategy for dealing with a high-salt form of environmental stress. The sugar-coat of *Pseudomonas* is more formally called an exo (that is, on the outside of the cell) polysaccharide (that is, a chain of sugars). The particular exopolysaccharide formed by *Pseudomonas aeruginosa* has been given the name "alginate."

Outside, away from the high salt environment of a human lung, *Pseudomonas* makes only a modest amount of alginate. This is important to its health, as high levels of alginate are toxic. Within the respiratory tract of a cystic fibrosis patient, by contrast, *Pseudomonas* makes a great deal more alginate, enough that cultured colonies have a "mucoid" appearance (colonies appear slimy). The thick alginate coat protects them from dessication in the high-salt environment, well worth the trade-off with danger of toxicity.

In order to insure that the situation does not get out of hand and too much alginate be produced, *Pseudomonas* has evolved a simple but elegant system of controls. Production of alginate is a complicated biochemical process governed by a master gene called *AlgU* that oversees alginate production by unleashing transcription of at least four gene promotors. In order to guard against runaway production of alginate, the *AlgU* master gene is subject to negative regulation by a cluster of four genes, *muc A,B,C,D* (that is, the proteins made by these genes stop *AlgU* from making alginate).

The role of *mucA*, *mucB*, and *mucD* in inhibiting alginate production by *AlgU* is easily demonstrated. Any mutation that disables one of these genes leads to increased alginate production. Most interestingly, however, mutation of *mucC* does not!

The role of *mucC* is thus somewhat of a mystery. To investigate it, Vojo Deretic at the University of new Mexico, Donald Rowen at the University of Nebraska, Omaha, and colleagues carried out an interesting series of investigations of how *mucC* influences *AlgU*'s production of alginate. To characterize high alginate production, they chose to look at its most visible result, the production of mucoid colonies. While inactivation of any of the other *muc* genes causes the production of mucoid colonies (presumably by releasing alginate production), inactivation of *mucC* does not. *mucC* colonies remain non-mucoid. What is going on here? Deretic's team set out to see.