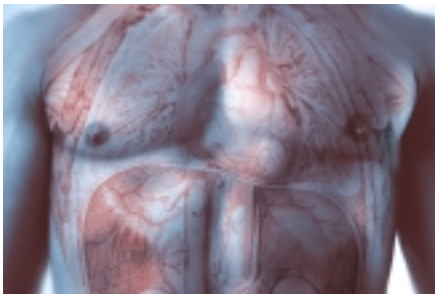
Therapeutic potential of a communication breakdown

Bea Perks, BMN News

Preventing bacteria from 'chatting' to one another presents a novel strategy to treat the potentially fatal lung infections that are characteristic of cystic fibrosis (CF), suggest US microbiologists. However, although the work marks an important advance, says a leading CF researcher, important questions remain.



Cellular communication

Researchers led by Laurance Rahme at Massachusetts General Hospital in Boston (http://www.mgh.harvard.edu/) have discovered that *Pseudomonas aeruginosa* bacterial cells communicate with one another using an intercellular signal belonging to a family of little known 4-hydroxy-2-alkylquinolines (HAQs).

Individual cells within many bacterial communities use so-called quorum sensing to communicate with one another and coordinate their behaviour almost as a 'pseudomulticellular organism', notes Rahme. But her latest data add an extra layer of complexity to the quorum-sensing model [1].

She has found that *P. aeruginosa* cells don't just send out and receive one signalling molecule, but engage in two-way conversations instead. One cell releases an HAQ precursor called 4-hydroxy-2-heptylquinoline (HHQ), and a second cell receives this and turns it into the HAQ signalling molecule.

'We want to understand the significance of chatting between the cells,' said Rahme. The extra level of complexity could help to increase the amount of information cells share with one another, she suggests, to improve synchronization of their behaviour.

'Such ... intercellular communication may be particularly important in chronic *P. aeruginosa* infections, including those of the lungs of CF patients because it is beneficial for bacteria to regulate their populations in such niches,' said Rahme. Chronic infection of the airways by *P. aeruginosa* is a common feature of CF pathogenesis and is strongly linked to impaired pulmonary function, pulmonary deterioration and mortality.

Treatment of infection

HAQ signalling is a potential target for the pharmacological treatment of these infections, says Rahme, and drugs developed with these targets in mind would have significant advantages over standard antibiotics. 'It is unlikely they will generate selective pressure for the inheritance of resistance,' she told *BioMedNet News* (http://gateways.bmn.com). The system is not essential for survival, she claims, so would not be selected for.

Rahme's work is important, says Jerry Pier, Professor of Microbiology at Brigham and Women's Hospital's Channing Laboratory (http://www.brighamandwomens.org), but the study only considered one *P. aeruginosa* strain. 'Until it is established that a significant number of clinical isolates produce these compounds and that they are required for virulence of most *P. aeruginosa* strains,' said Pier, 'the potential for treatment of *P. aeruginosa* infections by targeting these molecules is impossible to assess.'

Pharmaceutical companies have shown interest in targeting other molecules linked to quorum sensing in *P. aeruginosa*, says Pier. But he was recently involved in a study that concluded that only about 50% of clinical isolates of *P. aeruginosa* have a classic quorum sensing response as measured by transcriptional regulation of target genes.

Limitations

Rahme is certain her findings will apply across all *P. aeruginosa* strains. 'I do not believe this is a unique situation,' she said. All strains share the same genes for HAQ production, she says, adding that she sees no need to repeat her study on other strains.

But Pier is adamant. 'Until studies are extended to a wide range of clinical isolates, the utility of targeting quorum sensing systems in bacteria may be very limited,' he concluded.

Reference

1 Deziel, E. *et al.* (2004) Analysis of *Pseudomonas aeruginosa* 4-hydroxy-2-alkylquinolines (HAQs) reveals a role for 4-hydroxy-2-heptylquinoline in cell-to-cell communication. *Proc. Natl. Acad. Sci. U. S. A.* 101, 1339–1344

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