FAST MOVING FRONTS - 2010

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Paul Williams talks with *ScienceWatch.com* and answers a few questions about this month's Fast Moving Fronts paper in the field of Microbiology.

Article: Quorum sensing, communication and cross-kingdom signalling in the bacterial world
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Journal: MICROBIOLOGY-SGM, 153: 3923-3938 Part 12 DEC 2007
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SW: Why do you think your paper is highly cited?

This paper focuses on a "hot topic" in microbiology, namely 'quorum sensing,' i.e., the extraordinary capacity of unicellular microorganisms to behave socially by coordinating gene expression at the population level through the deployment of small diffusible signal molecules.

It provides a perspective primarily on N-acylhomoserine lactone AHL-mediated quorum sensing with a focus on prokaryotic-eukaryotic interactions and the specific responses of the latter to AHL signal molecules.

SW: Does it describe a new discovery, methodology, or synthesis of knowledge?

This paper is a synthesis of some of the quorum sensing research which my laboratory has undertaken for over almost the past 20 years, and for which I was awarded the Society for General Microbiology Colworth Prize Lecture, delivered at their 160th meeting on March 28th, 2007.

The article outlines my scientific contribution to the discovery of quorum sensing systems in diverse bacteria with a focus on plant-microbe interactions and the impact of quorum sensing signal molecules on the cells and tissues of higher organisms.

SW: Would you summarize the significance of your paper in layman's terms?

The discovery of the ubiquity of quorum sensing systems has completely changed the way in which we view microorganisms. No longer can we view bacteria as simple selfish individual cells striving only to divide and multiply.

We now appreciate that, for microbes, communication and teamwork are just as important as competition in the race to colonize new environmental niches, exploit available food resources, and combat threats such as predatory higher organisms and host immune defenses. With this new understanding come new opportunities for exploiting beneficial bacterial behavior and blocking adverse microbial activities.

"Quorum sensing systems are not only providing us with new fundamental insights into the social behavior of single and multiple species microbial communities but also provide new insights into evolutionary questions with respect to cooperation, communication, and altruism."

SW: How did you become involved in this research and were any particular problems encountered along the way?

In the late 1980s, I was working in collaboration with my colleagues Barrie Bycroft (at the University of Nottingham, UK) and George Salmond (then at Warwick University, UK) on the biosynthesis and regulation of carbapenem antibiotics in the plant pathogen, *Erwinia carotovora.*

Our strategic goal was to develop a biosynthetic alternative to the expensive industrial scale total chemical synthesis for this valuable class of antibiotics. By selecting for mutants unable to make the carbapenem, we hoped to identify the biosynthetic genes and gene products involved. Within this mutant bank, we identified a carbapenem-negative mutant class, in which antibiotic production could be restored by mixing with a second class of mutant.

Subsequent experiments revealed that the latter were producing a diffusible molecule which triggered antibiotic production in the former. After purifying a molecule which we presumed would be a biosynthetic intermediate, we were surprised to discover that it bore no structural resemblance to the carbapenem nucleus but instead was an AHL signal molecule, N-(3-oxohexanoyl)homoserine lactone (3O-C6-HSL).

On searching the literature, we discovered that 3O-C6-HSL was known and, in fact, was used by a completely unrelated marine bacterium (*Vibrio fischeri*) to regulate bioluminescence. For two such different terrestrial and marine organisms to share a common signalling molecule suggested we had stumbled upon something new and exciting: a widespread bacterial communication language.

We were able to quickly build on our serendipitous findings since we had, at the University of Nottingham, an international expert on bacterial bioluminescence, the late Gordon Stewart. He had constructed a light-based reporter system which could be exploited for the rapid screening of other bacterial species for the presence of 3O-C6-HSL.

This resulted in the discovery of many more AHL-producers, including important human pathogens such as *Pseudomonas aeruginosa.*

SW: Where do you see your research leading in the future?

Quorum sensing systems are not only providing us with new fundamental insights into the social behavior of single and multiple species microbial communities but also provide new insights into evolutionary questions with respect to cooperation, communication, and altruism.

A better understanding of the molecular nature of quorum sensing systems offers opportunities for harnessing beneficial bacterial community behavior or inhibiting pathogenic behavior; for example, in agriculture (control of plant pathogens and use of bacteria as biocontrol agents), medicine (as a means of diagnosis, or to monitor treatment), and industry (secondary metabolite production, microbial detection).

Quorum sensing systems in pathogens represent an exciting target for novel antimicrobials. These will attenuate virulence rather than kill, a feature which should hugely reduce the selective pressures associated with bactericidal agents which leads to the rapid emergence of resistance.

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