A brief on bacterial biofilms

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Many bacteria in nature and in persistent infections grow in communities on biofilms. A new study demonstrates that this adaptation is accompanied by a suprisingly modest change in the transcriptional profile of *Pseudomonas aeruginosa.*

It is now recognized that bacteria in nature and in many persistent infections grow as biofilms[1], involving colonial behavior of communities of bacterial cells on surfaces. These communities evolve subsequent to bacterial surface attachment and multiplication, and can be observed as structured 'heaps' of bacteria. Eventually, these may aggregate into mushroom-like shapes held together by the glycocalyx, an extracellular polysaccharide matrix[2].

Bacterial biofilms are relevant to events as apparently variable as the fouling of ships and the formation of chronic lung infections by *Pseudomonas aeruginosa* in people with cystic fibrosis—in which biofilm bacteria are more resistant to both antimicrobial treatment and host defense mechanisms. Because of these dramatic differences, it was generally assumed that there would be major differences in bacterial gene expression[1]. However, a paper by Marvin Whiteley and colleagues[3], appearing in a recent issue of *Nature*, provides a rather startling revelation. An assay of gene expression of *P. aeruginosa* indicates that, of the 5570 genes queried by genomic microarray[4], a rather modest number are up-regulated (34 genes) or down-regulated (39 genes) during biofilm growth. This represents a striking contrast to the change in expression of hundreds of genes induced by other conditions—for example, deficient Mg^{2+} in growth media (my unpublished observations).

It can be argued that this humble blip in expression levels may have something to do with the system used for growing biofilms (highly aerated, well-fed chemostat cultures containing sterilized granite pebbles as the substratum for biofilm growth). Indeed, biofilms often occur in nature under conditions of nutrient deprivation (for example, *Pseudomonas* attached to a rock in a stream) or other

stressful circumstances (such as a chronic lung infection treated with antibiotics). Despite its potential limitations, the study of Whiteley *et al.*[3] indicates a minimum subset of genes involved in specialized adaptation to biofilm growth; other genes found to be up- or down-regulated in other biofilms might reflect stimuli specific to the specific environments.

Observed changes in gene expression elicit speculation as to the biological consequence. Whiteley *et al.*[3] observed that bacterial flagellar and pili genes are downregulated in stable biofilms, even though they are known to be involved in the initial steps of biofilm microcolony formation[5]. Presumably, their downregulation reflects the fact that bacteria in biofilms are static (and thus no longer need flagella) and have alternative means of adhering to surfaces (the glycocalyx). Similarly, the downregulation of cytochrome oxidase might reflect a reduced requirement for aerobic metabolism in bacteria buried deeply within a microcolony. But the reasons for upregulation of the genes of defective temperate bacteriophage, or a series of ribosomal genes encoding 'hypothetical' proteins, remain obscure.

Also demonstrated is a change in expression of 20 genes induced by tobramycin treatment of *P. aeruginosa* biofilms (which are highly tobramycin resistant). The authors interpret these as being related to the development of phenotypic resistance to antibiotics, although this conclusion remains tentative.

Rather than dwelling further on the differences between solitary and communally-inclined *P. aeruginosa*, it seems appropriate to focus on the similarities: a change in expression of 98% of the genes is not affected by, or critical to, biofilm growth. Some constitutively-expressed genes may be necessary for biofilm formation, but overall, it seems that bacteria growing in biofilms are not that different from free-living bacteria. Understanding the genetics and biochemistry of this important biological process may be easier than hitherto imagined. □

Figure courtesy of Fiona S.L. Brinkman.

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