Ignoring signals and overgrowing others, two bacterial mutants

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When bacteria grow on agar medium they eventually run low on nutrition. Normally, bacteria upon sensing starvation stop growth and division to save the last nutrients. This stage in the growth cycle is called the stationary phase. Bacteria activate a physiological response that is typical for this situation. Thus, certain genes are turned on and other genes are turned off by the binding of the starvation-associated protein called sigma S, to RNA polymerase. RNA polymerase is the enzyme that transcribes DNA into RNA, which is in turn used as a template for protein synthesis.

While studying aging bacterial colonies it was discovered that some mutant cells within the colony ignore the "growth stop" signal and selfishly continue growing. Two classes of mutants have been found to have this 'growth advantage in aging colony' phenotype. In one mutant class the gene coding for sigma S was inactivated while in the other class a mutation in the *rpoB* gene made RNA polymerase resistant to the antibiotic rifampicin. Rifampicin-resistance comes from an amino acid change in RNA polymerase that is in close proximity to the binding site of the sigma S protein. The many different mutations that make bacteria resistant to rifampicin confer different degrees of growth advantage compared to the wild type. The mutant with sigma S inactivated confers a very strong growth advantage in aging colonies compared to the wild-type and to the Rif^R mutants.

Since RNA polymerase and sigma S physically interact to regulate transcription, and since both of these mutant classes confer a growth advantage in aging colonies, I asked the question whether they operated by a common mechanism. The hypothesis was that the growth advantage phenotype was caused by the absence of sigma S regulation, and that some rifampicin-resistance mutations in *rpoB* lowered polymerase interaction with sigma S, reducing the possibility for transcription regulation by sigma S and thus mimicking a sigma S mutant phenotype. To test this, the activity of sigma S-regulated genes was measured in strain carrying different rifampicin-resistance mutations associated with different levels of growth advantage.

Three rifampicin-resistant mutants, altering the same amino acid in RNA polymerase, gave a significant correlation between growth advantage in aging colonies and reduced expression of sigma S-regulated genes in stationary phase. These rifampicin-resistant mutants support the hypothesis that at least some growth advantage mutants mimic a sigma S mutant phenotype.

RNA polymerase and sigma S fit together like a key and a lock. The rifampicin resistant mutations in RNA polymerase could cause the "lock" to become sloppy, so that the key could fall off. Further experiments have to be conducted develop and further test this hypothesis.

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