BACTERIAL PHYSIOLOGY

A competent shut-down

In *Streptococcus pneumoniae*, the induction of competence, or the ability to take up DNA from the environment, is well characterized. A new paper now reveals how this process is switched off.

Competence in *S. pneumoniae* is induced during early exponential growth, when competence-stimulating peptide (CSP), encoded by *comC*, is sensed by a two-component system comprising the histidine kinase ComD and the response regulator ComE. Phosphorylated ComE (ComE-P) activates the early competence (*com*) genes, including *comCDE* and *comX*, which encodes σ^X. This competence-specific RNA polymerase σ-factor activates the late *com* genes, which encode the proteins involved in the uptake and chromosomal integration of the exogenous DNA.

> "competence is a transient process that stops as abruptly as it starts"

Although competence is a transient process that stops as abruptly as it starts, little information has been available on the mechanisms by which competence shuts down. Nicolas Mirouze, Mathieu Bergé and colleagues observed that cells lacking the DNA-processing protein DprA, a late *com* gene product which functions with the recombinase RecA in integrating the exogenous DNA, displayed altered competence kinetics. Inactivation of *dprA* increased the expression of *comX* but had little effect on the expression of *comC*. Expressing *dprA* as an early *com* gene under control of the *comC* promoter (P_{comC}) reduced transcription from the *comX* promoter but had no effect on transcription from P_{comC}. Taken together, these results suggest that DprA shuts off *comX* expression.

How does DprA mediate this effect? Yeast two-hybrid analysis revealed a strong physical interaction between DprA and a phosphoryl mimetic mutant of ComE, suggesting that DprA interacts with ComE-P. Further yeast two-hybrid analysis revealed that substitutions abolishing this interaction were clustered in the amino-terminal SAM domain of DprA, and introducing several of the corresponding mutations in the *dprA* chromosomal locus altered the shut-off of competence. DprA was also found to inhibit the binding of ComE to early *com* promoters *in vitro*. DprA therefore has a dual role in competence, being required both for RecA loading during DNA integration and for competence shut-off.

This study provides the first detailed look at how competence is switched off. Further work is required to decipher the specific mechanisms involved, but the authors speculate that DprA either acts as an anti-activator, preventing ComE-P binding to its target promoters, or interferes with ComE phosphorylation.

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ORIGINAL RESEARCH PAPER Mirouze, N. *et al.* Direct involvement of DprA, the transformation-dedicated RecA loader, in the shut-off of pneumococcal competence. *Proc. Natl Acad. Sci USA* 25 Feb 2013 (doi:10.1073/pnas.1219868110)