BACTERIAL PATHOGENESIS

sRNA clears the way for G4

DIGITAL VISION

In *Neisseria gonorrhoeae*, the pilus protein pilin undergoes antigenic variation through recombination of the *pilE* expression locus with various silent *pilS* loci in the genome. This results in variation in the protein sequence and expression levels of pilin, helping the bacterium to evade the host immune system. Previous work had shown that the *N. gonorrhoeae* chromosome contains 12 G·C base pairs upstream of *pilE* and that the G-rich strand of this region forms a guanine quartet (G4) structure that is essential for pilin antigenic variation. However, because G4 formation occurs only in single-stranded DNA, how this structure forms in the chromosomal duplex was unknown.

To investigate the mechanism of G4 formation, Cahoon and Seifert examined the DNA sequence around the G4 region. They identified a putative promoter between the G4 tract and *pilE*, oriented in the opposite direction to *pilE*, and showed that this promoter produced a low-abundance small RNA (sRNA) originating within the G4 region. Mutational inactivation of the sRNA promoter led to complete inhibition of pilin antigenic variation, indicating that transcription from this promoter is required for this process.

Insertions and deletions within the predicted sRNA sequence but downstream of the G4 region had no effect on antigenic variation, and the predicted sRNA sequence contained no ORF or ribosome-binding site, so the authors concluded that the sRNA is non-coding. Because transcription of the sRNA would be expected to melt the duplex DNA in this chromosomal locus and could therefore facilitate G4 formation, the authors reasoned that the sRNA acts in *cis*. Indeed, expression of the sRNA from another locus (without the neighbouring *pilE*) failed to restore antigenic variation in a mutant containing an inactive promoter at the endogenous sRNA locus.

The authors propose a model in which sRNA transcription from within the G4 sequence, and subsequent sRNA base-pairing with the C-rich strand, separates the DNA duplex, leaving the G-rich strand free to form the G4 structure and, thus, initiate pilin antigenic variation in an as-yet-unknown manner. Such a mechanism would mean that this sRNA does not fit the usual bacterial sRNA mould, as it acts on DNA instead of mRNA. However, a similar mechanism has been suggested to occur during immunoglobulin class switching, and it is possible that this model represents a more widespread system of transcriptionally induced, recombination-based gene conversion.

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ORIGINAL RESEARCH PAPER Cahoon, L. A. & Seifert, H. S. Transcription of a *cis*-acting, noncoding, small RNA is required for pilin antigenic variation in *Neisseria gonorrhoeae*. *PLoS Pathog.* **9**, e1003074 (2013)