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RNA WORLD

A new class of small RNAs

The identification of a novel class of small RNAs has provided specific insights into the function of this class, and indicates that this RNA species has a role in the DNA damage response by inhibiting protein translation.

The RNAi pathway is important for dsRNA-induced and transgene-induced gene silencing in the fungus *Neurospora crassa*. During their study of the regulation of the Argonaute protein QDE2, which is a component of the RNA-induced silencing complex in *N. crassa*, Lee and colleagues found that treatment with DNA-damaging agents increased QDE2 protein and mRNA levels.

By examining mutants in other components of the RNAi pathway, the authors found that QDE2 induction also required the RNA-dependent RNA polymerase (RdRP) QDE1, the DNA helicase QDE3 and the Dicer proteins DCL1 and DCL2. Because QDE1 and QDE3 are involved in generating dsRNA, the authors suggested that DNA damage could lead to the production of endogenous dsRNA species, which then activate *qde2* transcription. Indeed, they found that treatment with DNA-damaging agents led to the induction of a group of small RNAs associated with QDE2, which they named QDE2-interacting RNAs (qiRNAs). qiRNAs are 20–21 nucleotides in length, which is shorter than *N. crassa* siRNAs. Aberrant RNAs (aRNAs) — precursor small interfering RNAs that are specifically recognized by RdRPs to synthesize dsRNAs — were also induced in response to DNA damage.

What is the relationship between aRNAs and qiRNAs? The production of aRNAs was abolished in *qde3* mutants but accumulated in a Dicer mutant, which suggests that double-stranded aRNAs are precursors of qiRNAs. Surprisingly, knockout of *qde1* eliminated the induction of aRNAs in response to DNA damage, indicating that, in addition to its known role converting aRNA into dsRNA, QDE1 is also required for the synthesis of aRNAs. The authors found that QDE1 has a polymerase activity that uses both ssRNA and ssDNA templates, which suggests that as well as being an RdRP it also functions as a DNA-dependent RNA polymerase to transcribe aRNAs.

Do qiRNAs have a role in the DNA damage response? Most of the qiRNAs that were identified in this study originated from the ribosomal DNA locus, suggesting that they might affect ribosomal biogenesis. Consistent with this, protein synthesis was decreased in *N. crassa* after treatment with DNA-damaging agents, and this decrease was blocked in *qde1* and *qde3* mutants. The production of qiRNAs therefore seems to be a mechanism that contributes to DNA damage checkpoints by inhibiting ribosomal RNA biogenesis and protein synthesis.

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ORIGINAL RESEARCH PAPER Lee, H.-C. *et al.* qiRNA is a new type of small interfering RNA induced by DNA damage. *Nature* 14 May 2009 (doi:10.1038/nature08041).
FURTHER READING Ghiliyal, M. & Zamore, P. D. Small silencing RNAs: an expanding universe. *Nature Rev. Genet.* **10**, 94–108 (2009).

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