RNA INTERFERENCE

Silence restored

Certain yeast previously assumed to lack RNA interference machinery instead have alternative enzyme variants, which can in turn be transplanted to truly deficient species.

Although pathways for RNA interference (RNAi) exist in a vast array of species, they are notably absent from one of biology's favorite model organisms. "For a long time, people have known that there's no RNAi in *Saccharomyces cerevisiae*," says David Bartel of the Whitehead Institute, "and many people wanting to use the tools of budding yeast to study RNAi have lamented that this is the case."

All budding yeast apparently lack Dicer, an enzyme that processes double-stranded RNAs into small interfering RNAs (siRNAs), although some retain homologs of Argonaute, a key component of the RNA-induced silencing complex (RISC), and Bartel and colleagues were keen to explore whether 'Argonaute-only' yeast can perform RNAi.

They searched for candidate siRNAs in several species, including close *S. cerevisiae* relative *S. castellii*, and identified many molecules exhibiting hallmarks of Dicer-mediated cleavage from endogenous double-stranded RNAs. Although they could not identify canonical Dicer in these species, a more open-ended search for Dicer-like RNase III cleavage domains revealed a novel protein of apparently analogous function, which they named DCR1.

DCR1 lacks standard functional domains found in Dicer homologs from other species but is fully capable of partnering with Argonaute to facilitate RNAi. Even more striking, however, was the finding that transplanting the genes for DCR1 and Argonaute from *S. castellii* to *S. cerevisiae* was enough to render the latter strain fully RNAi-competent. "It's worked to knock down the expression of every gene we've tried to target," says Bartel.

In *S. castellii*, one job of the RNAi machinery appears to entail silencing of retrotransposons, and transplantation of these enzymes has the same effect in formerly RNAi-deficient yeast. "This result shows that the RNAi machinery can recognize transposons it hasn't seen before and specifically silence them but not the other genes of the cell," says Bartel.

These unexpected findings should expand the *S. cerevisiae* genetic toolbox, and Bartel's Whitehead colleague and collaborator Gerald Fink is also keen to apply RNAi to tackle pathogenic yeast *Candida albicans*, another DCR1-expressing strain that has proven challenging to study.

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RESEARCH PAPERS
Drinnenberg, I.A. *et al.* RNAi in budding yeast. *Science* advance online publication (10 September 2009).