RNA interference found in budding yeasts

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Some budding yeast species have the ability to silence genes using RNA interference (RNAi). Until now, most researchers thought that no budding yeasts possess the RNAi pathway because Saccharomyces cerevisiae, the protoypical model budding yeast does not.

RNAi, a key biochemical pathway in the genetic control networks of most organisms, has now been discovered in *Saccharomyces castellii*, a close relative of the prototypical budding yeast *S. cerevisiae*, and in Candida albicans, a common human pathogen.

Budding yeasts are used in research as models for more complicated organisms, in industry to create beer and biofuels, and in pharmaceuticals to produce drugs and vaccines. The ability to study RNAi in yeast and to use RNAi to alter the yeast's protein production may be beneficial for all these fields.

The finding is reported in the September 10 issue of *Science Express*.

"For a long time, people thought that budding yeast didn't have RNAi at all because Saccharomyces cerevisiae, which is the model budding yeast, doesn't have RNAi," says Kathleen Xie, an author on the paper and an undergraduate researcher in the lab of Whitehead Member David Bartel. "And this was kind of a pity because we didn't have a budding yeast model organism available for RNAi research."

Yeast is a good model for the cells of more complicated organisms, including humans, because yeast genomes are easy to manipulate, yeast

cells have a high rate of reproduction, and yeast cells have many functions and biochemical pathways in common with human cells.

One biochemical pathway found in more complex organisms is the RNAi pathway, which is used by plants and many animals to silence genes of viruses and transposons, which are parasitic DNA elements. Two key proteins involved in RNAi—known as Dicer and Argonaute—are lacking in the *S. cerevisiae* genome. However, the lab of Kenneth Wolfe at Trinity College, Dublin, found that other budding yeasts do have Argonaute, indicating that they might have some form of RNAi. Wolfe brought up the finding to Bartel, who has devoted most of his lab's effort to studying RNAi and related biochemical pathways.

Three Bartel researchers teamed up to determine whether any budding yeasts have RNAi capabilities, in collaboration with the laboratories of Wolfe and Whitehead Founding Member Gerald Fink. One of the species with the Argonaute protein is *S. castellii*. Anna Drinnenberg, a graduate student in the Bartel lab, developed *S. castellii* strains to study. Once the strains were established, Drinnenberg examined all of the small bits of RNA in *S. castellii* cells, looking for telltale signs that Dicer had been at work there.

Dicer, as its name implies, chops up long strands of double-stranded RNA into fairly uniform bits about 20 nucleotides long and hands them off to Argonaute. In *S. castellii* and in other budding yeasts, Drinnenberg found the correct size of chopped dsRNA in the yeast cells, yet was initially unable to detect a gene coding for a Dicer protein.

It turns out that the Dicer protein in these yeasts looks very different from the Dicer proteins of animals, plants and other fungi. "The fact that the Dicers of budding yeasts are so unusual probably explains why RNAi had gone undetected for so long in these species," says Bartel, who is also a professor at MIT and a Howard Hughes Medical Institute (HHMI)

investigator.

After the researchers confirmed that they had found the Dicer gene, David Weinberg, a graduate student in the Bartel lab, inserted the *S. castellii* Argonaute and Dicer genes into *S. cerevisiae*, which restored the RNAi pathway to this species that lost it.

Xie then observed that the restored RNAi pathway in *S. cerevisiae* prevented transposons from copying and reinserting themselves into the yeast's genome. Transposons can harm the genome, and one of the main purposes of the RNAi pathway in other species including animals is to silence them.

"With a validated Dicer protein in *S. castellii* and reconstituted pathway in *S. cerevisiae*, we can now examine an RNAi pathway using all of the tools available for studying budding yeasts," says Weinberg.

Bartel, agrees. "We can learn more about the RNAi pathway, just as yeast has taught us about many other biological processes. And there is a hope and assumption that researchers will now be able to use RNAi as a tool to learn more about these yeasts, including *C. albicans*."

For Fink, this research also beautifully models one of Whitehead's strengths--cooperation among researchers.

"This work was typical of collaboration at Whitehead," says Fink, "You do the experiments first and worry about acclaim afterward, so the outcome is more synergistic than if the labs worked independently."

Drinnenberg says that the teamwork was more than at the primary investigators' level. "Particularly in the initial steps in working with yeast, I would go downstairs to the Fink lab and the lab of Whitehead Fellow Andreas Hochwagen to ask for advice, and talking to the people

in their labs was very, very helpful."

More information: "RNAi in budding yeast", Science Express, September 10, 2009.

Source: Whitehead Institute for Biomedical Research (news : web)