



BRIEFS

Stanford researchers unmask proteins in telomerase

STANFORD, Calif.—Researchers at Stanford University School of Medicine have identified two new proteins that make up the telomerase complex and have a lead on several more. This is the first significant step toward understanding the makeup of telomerase since 1999, the researchers say, and the discovery of these two proteins provides new targets for cancer treatments. One of the more intriguing workhorses of the cell, the protein conglomerate called telomerase has been implicated in critical areas of medicine including cancer, aging and stem cell health. But researchers have been frustrated in their attempts to find the proteins that make up this complex. In their study, they describe two protein components of telomerase. They also show that disabling one of the proteins brings telomerase to a grinding halt. Although the work was done in cells in a lab dish, the findings suggest that a drug blocking that protein may be a useful tool against cancer.

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GENOMICS & PROTEOMICS

Putting the brakes on cancer?

Yale, Asuragen scientists show miRNA can reduce lung cancer growth

BY AMY SWINDERMAN

NEW HAVEN, Conn.—Researchers have found a miRNA molecule that substantially reduces cancer growth in multiple mouse models of lung cancer, the most common and deadly cancer worldwide.

The discovery, published in the March 15 issue of the journal *Cell Cycle* by researchers from the Yale University School of Medicine and Asuragen Inc., indicates a role for an miRNA in cancer progression and introduces a new therapeutic paradigm that features the treatment of cancer with a naturally occurring, small RNA.

The new finding demonstrates that a miRNA molecule known as let-7 inhibits the growth of lung cancer cells in culture and lung tumors in mice. Because multiple lung cancer cell lines and mouse models of lung cancer were used, it appears the therapeutic application of let-7 may provide benefits to a broad group of lung cancer patients.

"We believe our studies provide the first direct evidence in mammals that let-7 functions as a tumor suppressor gene and that this is the first report of a miRNA being used to a beneficial effect on any cancer," says senior author Frank Slack, associate professor of Molecular, Cellular and Developmental Biology at Yale.

David Brown, director of research at Asuragen, says the produc-



Frank Slack, a Yale associate professor, believes his university and Asuragen may be the first researchers to show a potential therapeutic in a miRNA, but says, "our story is just one tiny part of using miRNAs to combat cancer."

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Putting the brakes on cancer?

April 2008

by Amy Swinderman | [Email the author](#)[EDIT CONNECT:](#)

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STORY UPDATE

AUSTIN, Texas—Asuragen Inc. recently announced the launch of the first microRNA (miRNA) test for clinical diagnosis and disease management. The assay utilizes qRT-PCR technology* and differentiates between chronic pancreatitis and pancreatic cancer (pancreatic ductal adenocarcinoma). Pancreatic cancer is the 4th leading cause of cancer related deaths in the United States. Chronic pancreatitis and pancreatic cancer present similar symptoms and can be mis-diagnosed in up to 25% of patients. The test was developed following the discovery of novel microRNAs associated with pancreatic cancer in collaboration between Asuragen scientists and Dr. Stephan Hahn and colleagues at Ruhr University, Bochum, Germany as reported in the journal *Oncogene* in 2007.

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David Brown, director of research at Asuragen, says the productive industry-academic collaboration provides additional support for miRNA replacement therapy as an important component of effective cancer treatment regimens in the future.

"With the down-regulation of miRNAs at the core of the development of many cancers, this finding may be a key modality for preventing or eliminating the spread of the disease," Brown notes.

The finding has already spurred Asuragen into action. On April 3, the company announced the launch of [Mirna Therapeutics](#), a new company focused on the development and commercialization of miRNA oncology therapeutics.

Asuragen is transferring its miRNA therapeutic intellectual property to Mirna Therapeutics and seeding the new company with \$3 million in capital. Mirna Therapeutics will operate as an independent company with its own management team and board of directors.

The researchers' finding was more than 10 years in the making. Slack's research group initially discovered the let-7 miRNA in *C. elegans*. Slack's team began examining the role of their human homologues in disease. Slack discovered that among the genes regulated by let-7 in *C. elegans* are several genes related to cancer, including the homologue of the human cancer gene, RAS.

"When we looked for genes being targeted by let-7, the miRNA appeared to be binding to the RAS gene. We were able to show that let-7 decreased its expression in multiple kinds of cancer, but particularly in lung cancer," Slack says.

Slack shared these findings at a fateful appearance in April 2004 at the Keystone Symposium, "siRNAs and miRNAs," in Keystone, Colo. In the audience sat Brown, attending the seminar on behalf of Asuragen, which was using miRNA expression analyses in lung tumors and miRNA functional studies in lung cancer cell lines to identify miRNAs with therapeutic potential.

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"I ended my presentation by saying, 'I wouldn't be surprised if somebody calls me tomorrow to tell me they identified let-7 in cancer,'" Slack says.

"It took me about two days to get back to the office and figure out how to contact him, but I did," Brown says.

Before long, several scientists at Asuragen teamed up with the Slack lab to study the tumor suppressor activity of let-7. Human lung cancer cells were treated with a negative control miRNA or a mimetic for a miRNA commonly down-regulated in the tumors of lung cancer patients. The cells were injected into mice and allowed to form tumors.

Tumors that developed from the cells treated with the cancer-specific miRNA mimetic appeared much later than tumors from cells treated with a corresponding negative control miRNA mimetic. Histological staining of tumors taken more than two weeks after treatment with the miRNAs revealed significantly fewer cancer cells and lower proliferation in tumors treated with the therapeutic miRNA than those treated with the negative control.

"Our paper might be the first to show a potential therapeutic in an miRNA," Slack says, "but our story is just one tiny part of using miRNAs to combat cancer. I think this will stimulate us to do more preclinical trials to determine if we can use this particular molecule against more aggressive forms of cancer."

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