

## Small molecule may help pinpoint some cancers

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In recent years, scientists have begun to catalog an astonishing array of small, distinct genetic elements that seem to play an important role in how genes function.

Known as microRNAs for their Lilliputian dimensions - just 22 nucleotides long - they have generated much excitement among scientists, as they seem to be ubiquitous in nature, working in both plant and animal cells.

According to University of Wisconsin-Madison Medical School Professor James Dahlberg, within only the past five years or so have scientists begun to understand the ways that microRNAs mediate gene expression, taking part in the complicated genetic interplay that governs many life processes.

Now, writing in the March 8 issue of the Proceedings of the National Academy of Sciences (PNAS), groups led by Dahlberg and his collaborator Wayne Tam, at the Joan and Sanford I. Weill Medical College of Cornell University, report that elevated cellular levels of a particular microRNA, known as miR-155, may be diagnostic of some human cancers, notably lymphomas.

In particular, Dahlberg says, the elevated presence of the molecule may help clinicians distinguish between types of lymphoma that have different outcomes. "Monitoring the levels of miR-155 could help differentiate between these forms," Dahlberg explains. So the discovery by the Dahlberg and Tam groups may have value in diagnosis of cancers that are difficult to distinguish in other ways.

Cells have several hundred different kinds of microRNA. Normally, miR-155 is present in about 200 copies per cell, but it was found to rise to more than 10,000 in some of the lymphomas analyzed in this study. The precise role of this microRNA in lymphoma remains to be worked out.

Scientists are just beginning to tease out the roles of microRNAs, which act by directing silencing factors to certain messenger RNAs (information-containing molecules). "The result is that microRNAs reduce the synthesis of proteins from specific messenger RNAs," says Dahlberg. "The messenger RNA targets of miRNA-155 in the lymphomas are unknown, but there are several good candidates."

A cancer can be viewed as tissue that has undergone an aberrant type of development. "MicroRNAs affect normal development, so abnormal amounts of microRNAs could make them grow in an uncontrolled or inappropriate manner," says Dahlberg.

"Cancers usually result from several problems in a cell, with no single agent being totally responsible," he explains. "So any effects of miR-155 are likely to be part of a bigger picture, where other things have also gone wrong in the cell."

This is the first report of a microRNA increasing in amount in cancer, which may help scientists understand what changes normal cells into lymphoma cells.

In addition to Dahlberg and Tam, authors of the PNAS paper include Peggy S. Eis and Elsebet Lund of UW-Madison, and Liping Sun, Amy Chadburn, Zongdong Li and Mario F. Gomez of Cornell Medical School.

Dahlberg and Lund own stock in Third Wave Technologies, a company

that was co-founded by Dahlberg and that manufactures some of the chemicals used in this work.

Source: UW-Madison

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