DMS's Laura Barre, M.D., studied 183 older adults and found they were at higher risk of frailty (such as weight loss, weakness, or low activity) if they had a serious mental illness.

Rogue molecule is linked to lung cancer

A tiny snippet of RNA promotes lung cancer in mice and men, Dartmouth researchers have discovered. MicroRNAs (miRNAs) are small RNA molecules that regulate gene expression. "They were originally discovered as playing critical roles in development," says Ethan Dmitrovsky, M.D., DMS's Andrew G. Wallace Professor of Pharmacology and Toxicology.

The first miRNA was discovered in 1993. Since then, hundreds more have been described. They can degrade or impair messenger RNA, putting the brakes on protein production. In healthy cells, this plays a role in regulating the expression of genes. But when the process goes haywire, it can lead to disease, including lymphoma, leukemia, colon cancer, and breast cancer.

Dmitrovsky's team has identified one miRNA, miR-31, that causes lung cancer when it goes rogue. The finding appeared in the *Journal of Clinical Investigation*.

Lab: Xi Liu, Ph.D., now a postdoctoral fellow at the National Cancer Institute, headed up the study as a graduate student in Dmitrovsky's lab. First, the team engineered a mouse to overexpress a human protein in its lungs. The protein, cyclin E, is known to play a role in human lung cancer. As planned, the engineered mice went on to develop "many features of human lung cancer," Dmitrovsky says.

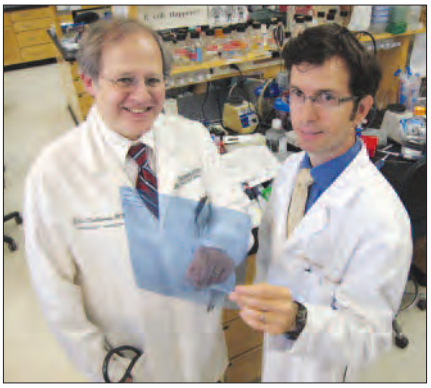
Tissue: The researchers then set out to look for miRNAs that were expressed more strongly in cancerous tissue from the engineered mice than in healthy mouse lung tissue. Ten molecules stood out. The team examined whether those 10 miRNAs were also overexpressed in samples of human lung cancer tissue. "Of the 10, we found three that were prominently overexpressed in both mouse and human lung cancer," Dmitrovsky explains. None of the three had previously been linked to lung cancer.

None of the miRNAs had previously been linked to lung cancer.

These results were promising, but the researchers were just getting warmed up. Next, they experimentally overexpressed and repressed levels of those three miRNAs to see what would happen. "We found only one, miR-31, that was cancer causing," Dmitrovsky says. When its expression was ramped up, tumors grew. When its expression was knocked back, cancer growth was significantly reduced in both mouse and human cell lines.

Pathway: Looking still deeper, the team identified genes involved in the cancer-causing pathway. They found that miR-31 inhibits two tumor-suppressor genes, allowing lung cancer to grow. "This would imply that targeting miR-31 represents a potential treatment for lung cancer," Dmitrovsky says.

That, not surprisingly, is where his research is headed next—to see if modified forms of miR-31 can be used to inhibit the growth of lung cancer. "This is a new and evolving field," Dmitrovsky says. The field may be green, but he and his colleagues are making significant strides in understanding how tiny pieces of RNA can wreak havoc on cells—and how to keep that from happening. KIRSTEN WEIR



JUNIPER TRAILS

Dmitrovsky, left, and Lorenzo Sempere, a research associate in his lab, continue to study miR-31.

Sensational study

A DMS-led team assessed if teenagers who exhibit sensation seeking—the "tendency to seek out novel and exciting stimuli"—are more likely to start drinking or smoking. They surveyed adolescents aged 10 to 14 and used a series of questions to rate their sensation-seeking tendencies. The team reported in *Addiction* that "sensation seeking was found to be a moderately strong predictor of binge drinking and a strong predictor of established smoking." The authors argue that interventions to prevent binge drinking and smoking among adolescents should primarily target sensation seekers.

A PSA about PSA screening

"There is growing concern that older adults are at risk for exposure to potentially harmful treatments for which the promised benefit is small, if not absent," wrote Julie Bynum, M.D., and her coauthors in the *Journal of the American Geriatrics Society*. They examined rates of prostate-specific antigen (PSA) screening in men 80 and older. PSA testing can signal a risk of prostate cancer but also involves potential harms and, in some populations, a low likelihood of benefit. Bynum found that rates of screening in this age group varied from 2% to 38% and that regions with higher rates had higher overall Medicare expenditures. ■