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MicroRNA molecule found to be a potent tumor-suppressor in lung cancer

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New research shows that microRNA-486 is a potent tumor-suppressor molecule in lung cancer, and that the it helps regulate the proliferation and migration of lung-cancer cells, and the induction of programmed cell death, or apoptosis, in those cells.

The preclinical study was led by researchers at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James). It found that microRNA-486 (miR-486) directly targets the insulin growth-factor pathway, which is important for cell survival and proliferation. Alternations in the pathway are believed to play an early role in tumor initiation and progression.

The researchers further found that miR-486 is itself regulated by the tumor-suppressor gene p53, the most frequently altered gene in human cancers, and that activity of miR-486 is partially dependent upon functional p53.

Published in the *Proceedings of the National Academy of Sciences*, the study suggests that miR-486 might serve as a biomarker for lung-cancer patients who might respond to treatment with insulin-growth-factor inhibitors.

"It wasn't known whether miR-486 functioned as an oncogene or a tumor-suppressor gene in lung cancer," says co-corresponding author Patrick Nana-Sinkam, MD, associate professor of medicine and a

researcher with the OSUCCC – James Molecular Biology and Cancer Genetics Program.

"miR-486 appears to be a biomarker for lung cancer, but its mechanisms of action remain unclear," he says. "These findings show that miR-486 serves a tumor-suppressor function in lung cancer, and that miR-486 action is partially dependent on p53."

"This partial reliance of one tumor-suppressor on another was a surprise," says principal investigator and co-corresponding author Carlo M. Croce, MD, director of Ohio State's Human Cancer Genetics program and the John W. Wolfe Chair in Human Cancer Genetics at the OSUCCC – James. "We don't know yet what implications, if any, this might have for the development of targeted therapies."

MicroRNAs are a class of short, non-coding RNAs that regulate the translation or degradation of messenger RNA and therefore the proteins that cells make. Research is showing that certain microRNAs are frequently dysregulated in cancer.

Nana-Sinkam and his colleagues examined lung-tumor samples from 81 patients with stage-1 nonsmall-cell lung cancer and tumor-cell lines. Analyses identified miR-486 as the most decreased of microRNAs in the cells, so the researchers chose it for further investigation.

Provided by Ohio State University Medical Center