Molecule blocks gene, sheds light on liver cancer

August 1 2007

New research shows how a particular small molecule blocks the activity of a cancer-suppressing gene, allowing liver-cancer cells to grow and spread.

This molecule is a microRNA, a recently discovered class of tiny molecules used by cells to help control the kinds and amounts of proteins they make. More than 250 different microRNAs have been discovered, and several have been linked to cancer.

These findings show exactly how one specific microRNA, called miR-21, helps cancer develop.

This molecule occurs at unusually high levels in many kinds of cancer cells. The study looked at a gene called PTEN (pronounced P-TEN), which normally protects cells from becoming cancerous. Researchers know that the abnormal silencing of this tumor-suppressor gene contributes to the development of liver cancer and other malignancies.

The findings help explain how liver cancer develops and may identify new drug targets for treating the disease. This particular microRNA might also provide a marker to help determine a patient's prognosis.

The study, led by researchers at the Ohio State University Comprehensive Cancer Center, is published in the August issue of the journal *Gastroenterology*.

“Our findings essentially describe a new mechanism used by cells to regulate PTEN,” says principal investigator Tushar Patel, professor of internal medicine, director of hepatology and a liver-cancer specialist at Ohio State University Medical Center.

They show that high levels of miR-21 block the PTEN gene, he explained. This, in turn, activates chemical pathways that enable cancer cells to proliferate, migrate and invade other tissues, all of which are features of tumor formation.

Patel and his collaborators began the study by measuring the relative levels of 197 microRNAs in normal liver cells and in liver cancer cells from human tumors and in four liver cancer cell lines.

Levels of miR-21 were up to nine times greater in liver-tumor tissue compared with normal liver tissue, twice that of the next highest microRNA.

Earlier research led by Patel had shown that miR-21 probably targeted PTEN, and this study confirmed that.

Furthermore, the researchers showed that adding high levels of miR-21 to normal liver cells caused PTEN levels to drop. They also traced the chemical pathways that increased the cells' abilities to proliferate, migrate and invade other tissues.

“Our findings indicate that miR-21 plays a fundamental role in tumor-cell behavior and cancer development,” Patel says, “and this may also be relevant to other tumors in which miR-21 is overexpressed. If this work is reproduced in investigations of other cancers, it could be a big step forward,” he says.

Source: Ohio State University