UT SOUTHWESTERN MEDICAL CENTER NEWS

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Lung cancer culprit could offer target for therapy, UT Southwestern researchers report

DALLAS – Sept. 13, 2010 – A tiny molecule that spurs the progression of non-small-cell lung cancer could become a player in fighting the disease, say researchers at UT Southwestern Medical Center, who published a study on how the molecule behaves in mice in the Sept. 14 issue of *Cancer Cell*.

Scientists have known that the molecule microRNA-21, or miR-21, is present in overabundant quantities in human tumors, including non-small-cell lung cancer (NSCLC). Until now, however, it was unclear whether miR-21 contributed to the development of lung cancer, or whether it was simply an indicator of the presence of the disease.

To find out, lead study author Dr. Mark Hatley, an instructor of pediatric hematology/oncology, and UT Southwestern colleagues used mice that had been altered specifically to harbor non-small-cell lung cancer. In some of these mice, they genetically engineered the animals to produce too much miR-21. In another group, they deleted the *miR-21* gene altogether, which eliminated the molecule in the rodents.

In animals with cancer, the results showed that too much miR-21, or overexpression, promotes the formation, growth and survival of new tumors by turning off certain genes that normally allow cancer cells to die. In fact, at 18 weeks of age, the study group with overexpressed miR-21 had significantly more tumors than their lung-cancer-carrying littermates with normal levels of miR-21. Healthy rodents engineered to overexpress miR-21 did not develop cancer.

"These results indicate that overexpression of miR-21 alone is not enough to initiate tumors in a healthy animal. Instead, it appears that miR-21 enhances the growth and survival of existing lung cancer," said Dr. Hatley, a Pediatric Scientist Development Program Fellow sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

Dr. Eric Olson, chairman of molecular biology at UT Southwestern and the study's senior author, said the experiments also show that deleting miR-21 sensitizes the animals' cancer cells to a certain kind of chemotherapy, suggesting that inhibiting miR-21 in lung-cancer patients could be of therapeutic value.

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"Methods currently exist to pharmacologically manipulate molecules like miR-21," said Dr. Olson, who directs the Nancy B. and Jake L. Hamon Center for Basic Research in Cancer and the Nearburg Family Center for Basic and Clinical Research in Pediatric Oncology. "More research will be needed before we know whether this is applicable to humans, but it's possible that a drug designed to inhibit miR-21 could help keep cancer at bay."

MiR-21 is a type of molecule called a microRNA. These small snippets of RNA – the chemical cousin of DNA – normally help coordinate and regulate the production of specific proteins in cells. When miRNAs go awry, however, diseases such as cancer can result.

Other UT Southwestern researchers involved with the study were David Patrick, graduate student; Matthew Garcia, research technician; Dr. James Richardson, professor of pathology, molecular biology and plastic surgery; Dr. Rhonda Bassel-Duby, professor of molecular biology; and Dr. Eva Van Rooj, adjunct instructor in molecular biology.

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