MedicalXpress

Scientists define important gene interaction that drives aggressive brain cancer

December 11 2014

Targeted therapies are a growing and groundbreaking field in cancer care in which drugs or other substances are designed to interfere with genes or molecules that control the growth and survival of cancer cells. Now, scientists at Virginia Commonwealth University Massey Cancer Center and VCU Institute of Molecular Medicine (VIMM) have identified a novel interaction between a microRNA and a gene that could lead to new therapies for the most common and deadly form of brain tumor, malignant glioma.

In a study recently published in the journal *Neuro-Oncology*, a team of scientists led by Luni Emdad, M.B.B.S., Ph.D., and Paul B. Fisher, M.Ph., Ph.D., provided the first evidence of an important link between a specific microRNA, miR-184, and a cancer promoting gene, SND1, in the regulation of malignant glioma. miR-184 is known to suppress tumor development by regulating a variety of genes involved in cancer growth, while SND1 has been shown to play a significant role in the development of breast, colon, prostate and liver cancers. Through a variety of preclinical experiments, the team demonstrated that increasing the expression of miR-184 slows the growth and invasive characteristics of glioma cells through direct regulation of SND1. Additionally, they showed that reduced levels of SND1 led to reduced levels of STAT3, a gene that has been shown to promote the most lethal characteristics of brain cancer.

"Patients suffering from brain tumors are in desperate need of improved therapies," says Fisher, Thelma Newmeyer Corman Endowed Chair in

Cancer Research and co-leader of the Cancer Molecular Genetics research program at VCU Massey Cancer Center, chairman of the Department of Human and Molecular Genetics at VCU School of Medicine and director of the VIMM. "We're hopeful that this new understanding of the relationship between miR-184 and SND1 ultimately will lead to the development of new drugs that reduce SND1 expression and improve patient outcomes."

Prior studies have shown that levels of miR-184 are unusually low in tissue samples from patients with malignant gliomas. Using advanced computer analysis techniques designed to study and process biological data, the researchers identified SND1 among a handful of other genes that miR-184 helps regulate. Knowing SND1 is implicated in a variety of cancers and having previously defined its role in liver cancer, Emdad, Fisher and their colleagues explored this relationship further. They confirmed low levels of miR-184 expression in human glioma tissue samples and cultured cell lines as well as an increase in the expression of SND1 compared to normal brain tissue. Using data from a large public brain tumor database called REMBRANDT, the researchers confirmed that patients with lower levels of SND1 survived longer than those with elevated SND1 expression.

"We still have a long way to go and many challenges to overcome before we will have therapies that are ready for clinical use, but this is a significant first step in the process," says Emdad, member of the Cancer Molecular Genetics research program at Massey, assistant professor in the VCU Department of Human and Molecular Genetics and member of the VIMM. "Future studies will aim to explore the relationship between SND1 and STAT3, identify additional microRNAs that may be relevant to malignant glioma and explore the effects of drugs that block SND1 expression in more advanced preclinical models."

More information: The full manuscript of this study is available