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Novel RNA interference screening technique identifies possible path for malignant glioma treatment

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Researchers at the University of Massachusetts Medical School report in the journal *Nature Medicine* on a cellular pathway in the deadly brain cancer malignant glioma, a pathway essential to the cancer's ability to grow - and a potential target for therapy that would stop the cancer's ability to thrive.

In the paper "A genome-wide RNA interference screen reveals an essential CREB3L2-ATF5-MCL1 survival pathway in malignant glioma with therapeutic implications," appearing this week as an Advanced Online Publication, UMass Medical School Professor Michael R. Green, MD, PhD, and colleagues use a genome-wide RNAi screening tool to identify a dozen genes that affect the function of a crucial protein necessary for glioma cells to grow; further research found a key pathway that appears in laboratory cultures and mouse models to be susceptible to two cancer drugs already in use for other types of cancer.

A hallmark of cancer is uncontrolled cell growth, often caused by overexpression of genes that help cells survive, or underexpression of those genes that induce normal cell death. Genes that are expressed highly in cancer cells and are essential for their survival are appealing targets for drug therapy.

Green's lab has in recent years developed a clever way of scanning the genome to identify genes that appear to promote the natural process of

programmed cell death called "apoptosis", or that inhibit the growth of cells; Green and colleagues used a technique called genome-wide RNA interference screening—to identify novel genes that regulate the expression of a transcription factor called ATF5 in malignant glioma cells. The discovery of at least one previously unknown genetic pathway that appears to regulate this key transcription factor, and the subsequent determination that the cancer drugs sorafenib and temozolomide inhibit glioma growth point to dramatic new possibilities for potential therapeutics and are exciting advances at the frontier of cancer biology and genetic expression.

ATF5 was first identified as an important pro-survival factor by Dr. Green in 2002.

Provided by University of Massachusetts Medical School