

New target identified for potential brain cancer therapies

January 13 2015

Researchers from Virginia Commonwealth University (VCU) Massey Cancer Center and the VCU Institute for Molecular Medicine (VIMM) have identified a new protein-protein interaction that could serve as a target for future therapies for the most common form of brain cancer, glioblastoma multiforme (GBM). GBM is a devastating disease that originates from glia or their precursors within the central nervous system, and the prognosis for GBM patients is unfortunately poor, but this discovery offers new therapeutic potential.

According to a new study recently published in the online edition of the journal *Cancer Research*, scientists pinpointed a novel interaction between the genes AEG-1 and Akt2 that regulates the malignant characteristics of GBM. Prior research by the study's lead author, Paul B. Fisher, M.Ph., Ph.D., discovered the AEG-1 gene and found it to be overexpressed in the vast majority of cancers. The Akt2 gene is also overexpressed in several additional cancers. This new research demonstrates a positive feedback loop between the proteins expressed by these genes that promote GBM growth and survival.

"This is the first time that this specific protein-protein signaling complex has been identified in GBM, and it gives us a new potential target for drug development," says Fisher, Thelma Newmeyer Corman Endowed Chair in Cancer Research and co-leader of the Cancer Molecular Genetics research program at VCU Massey, professor and chair of the Department of Human and Molecular Genetics at the VCU School of Medicine, and director of the VIMM. "If we can develop drugs that

disrupt the interaction between these two proteins, we could potentially combine them with conventional therapies to more effectively treat malignant gliomas."

Cell signaling is a complex process where interactions between cells and their environment govern basic cellular functions and activities. Bin Hu, PhD, senior postdoctoral scientist on Fisher's team discovered that the interaction between the AEG-1 and Akt2 proteins was critical for further Akt2 signaling, which regulates tumor cell survival, proliferation and invasion.

Additionally, analyses of patient tissue samples showed that AEG-1 and Akt2 expression correlated with GBM progression and reduced patient survival. In preclinical experiments, the researchers disrupted AEG-1/Akt2 interaction through a process known as competitive binding and observed a reduction in GBM cell survival and invasion. When combined with AEG-1 silencing in mouse models of human GBM, there was a marked increase in survival.

"In this study we mapped the interacting regions in both genes in order to begin the process of developing drugs that can fill in these spaces and block the genes from binding," says Fisher. "If successful, these new treatments could also be applicable to a variety of additional cancers in which both genes are overexpressed."

More information:

cancerres.aacrjournals.org/content/74/24/7321.long

Provided by Virginia Commonwealth University

Citation: New target identified for potential brain cancer therapies (2015, January 13) retrieved

19 April 2024 from

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