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Researchers identify role of gene in tumor development, growth and progression

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Virginia Commonwealth University Massey Cancer Center and VCU Institute of Molecular Medicine researchers have identified a gene that may play a pivotal role in two processes that are essential for tumor development, growth and progression to metastasis. Scientists hope the finding could lead to an effective therapy to target and inhibit the expression of this gene resulting in inhibition of cancer growth.

According to Paul B. Fisher, M.Ph., Ph.D., professor and chair of the Department of Human and Molecular Genetics, director of the VCU Institute of Molecular Medicine in the VCU School of Medicine, and program leader of Cancer Molecular Genetics at the Massey Cancer Center, the team has shown that astrocyte elevated gene-1, AEG-1, a cancer promoting gene, is involved in both oncogenic transformation, which is the conversion of a normal cell to a cancer cell, and angiogenesis, which is the formation of new blood cells. Oncogenic transformation and angiogenesis are critical for tumor development, growth and progression to metastasis.

In the study published online the week of Nov. 16 in the Early Edition of the journal *Proceedings of the National Academy of Sciences*, researchers employing a series of molecular studies reported that the elevated expression of AEG-1 is involved with turning normal cells into cancer cells.

According to Fisher, when AEG-1 was expressed in normal immortal rat embryo fibroblast cells it converted these cells into transformed cells

that induced rapidly growing aggressive cancers when injected into animals. AEG-1 expressing cells displayed enhanced expression of genes regulating blood vessel formation, thereby contributing to tumorigenicity. The team has further defined the pathways in target cells that are activated by AEG-1 and mediate its oncogenic and angiogenic inducing properties.

"Our goal is to understand the functions of a novel gene AEG-1 that plays an essential role in tumor progression, with potential to develop effective therapeutic approaches for multiple cancers through targeted inhibition of this novel molecule or its downstream regulated processes," said Fisher, who is the first incumbent of the Thelma Newmeyer Corman Endowed Chair in Cancer Research with the VCU Massey Cancer Center.

"We believe it will pave the way for ameliorating the sufferings of scores of cancer patients by uncovering new and effective avenues for treatment," he said.

To expand the work on AEG-1, the VCU Department of Human and Molecular Genetics, Institute of Molecular Medicine and Massey Cancer Center recently received a National Cancer Institute grant totaling $1.6 million to study the AEG-1 gene in the context of malignant brain tumors such as glioblastoma multiforme, or GBM. According to Fisher, who is the primary investigator for the study, the work will extend the understanding of this gene and how it may serve as an oncogenic, or transforming gene.

"Cancer development and progression are multi-factor and multi-step processes that occur in a temporal manner. As mentioned above AEG-1 clearly has multiple roles in various steps of tumor progression, including tumor cell growth, insensitivity to growth-inhibitory signals, including chemotherapeutic agents, invasion, angiogenesis and metastasis,"

explained Fisher.

"In addition, AEG-1 has been known to have oncogenic roles in various cancers including glioma (CNS tumor), neuroblastoma, liver cancer, breast cancer, prostate cancer, lung cancer, and esophageal squamous cell carcinoma. These important correlations make this gene an intriguing molecule to study with potential to serve as a direct target for cancer therapy," he said.

The gene was discovered in 2002 in Fisher's laboratory while he was at the Columbia University College of Physicians and Surgeons in New York.

Source: Virginia Commonwealth University (news : web)