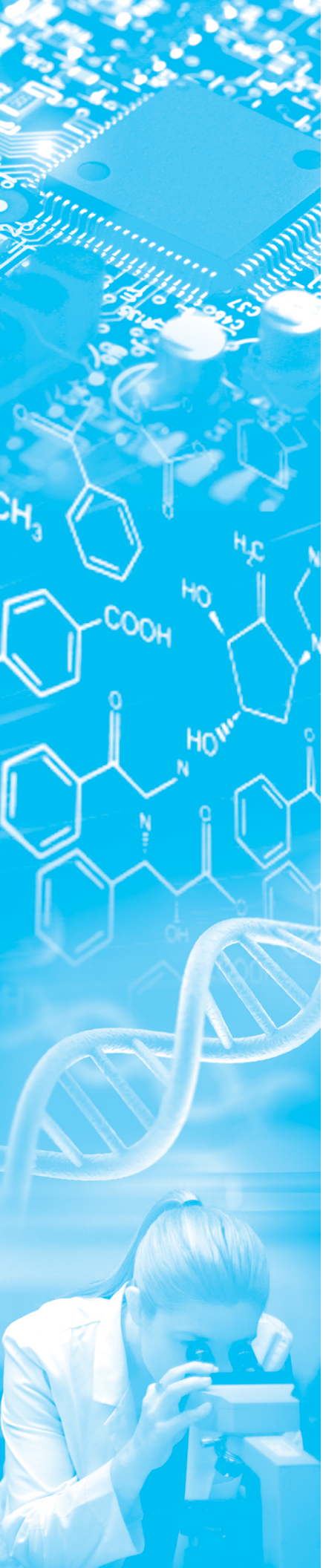

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Anti-VEGF Small Molecule for Treating Brain Cancer

Each year millions of people are diagnosed with cancer and one of the most prevailing and lethal forms is brain cancer. It is the leading cause of cancer related deaths among children and third most common cause of cancer related death among patients aged 15 - 39. All brain cancers are not the same and they are classified into 12 main groups and over 100 subgroups depending upon their biological features. One of these types, called gliomas, are brain cancers that arise from the connective tissue of the brain. Gliomas account for 74% of malignant brain cancers and are one of the most aggressive forms. Among them, glioblastoma multiforme (GBM) is the most common and lethal form of glioblastoma and despite the development of various anticancer drugs, success against GBM has been limited. Currently, patients with GBM have poor five-year survival rate of only 5% and median survival post-diagnosis is merely about one year. Hence there is a serious need for developing novel treatments for this malignancy. GBM is characterized by increased vasculature and blood vessel growth around the tumor is essential for its survival. The abnormal vasculature associated with GBM is believed to enhance hypoxia and impair delivery of chemotherapeutic agents. Considering the dependence of GBM on angiogenesis, researchers at NSU's Rumbaugh-Goodwin Institute for Cancer Research developed a therapeutic strategy against GBM that utilizes inhibition of blood vessels in the tumor microenvironment.

Technology

The technology is a therapeutic method that implements the use of a small molecule, codenamed F16, which binds to and inhibits the Vascular Endothelial Growth Factor-2 (VEGF) receptor and prohibits angiogenesis. Therefore, it slows down or prevents formation of vasculature essential for the tumor's survival and starves the cancer to death. Passing through the blood-brain-barrier (BBB) is a major obstacle for therapeutic molecules used to treat brain cancers such as GBM. Owing to the relatively small molecular size of F16, it can traverse the BBB as demonstrated by its efficacy against *in vivo* GBM mouse models. In preliminary *in vitro* and *in vivo* experiments, F16 was demonstrated to have both anti-angiogenic and pro-apoptotic properties, making it an ideal candidate for treating a brain cancer such as GBM whose survival and growth is reliant upon increased vasculature development. Efficacy of F16 in treating brain cancer and secondary toxic effects were tested and compared with currently used chemotherapy drugs temozolomide and paclitaxel. In these preclinical studies, F16 demonstrated better or equivalent efficacy and less secondary toxicity compared with both chemotherapy drugs. Thus, F16 provides a new treatment modality for brain cancers such as GBM.

Application

- This novel technology can be used to treat GBM for which prognosis is poor.

- Currently the treatment regimen for GBM yields poor survival rate and produces significant toxic side effects. F16 has the potential to improve treatment efficacy with diminished adverse events.
- F16 has also demonstrated success against other forms of solid tumors.

Advantages/Benefits

- Development of vasculature is essential for GBM, therefore an anti-VEGF molecule that acts as an angiogenesis inhibitor is an ideal candidate for treating GBM.
- Results of *in vivo* experiments demonstrated that treatment by F16 resulted in less secondary toxicity compared to currently used chemotherapy drugs such as paclitaxel.
- Owing to its relatively smaller molecular size unlike most currently used therapeutic agents, F16 can breach the BBB, making it ideal for targeting brain cancers.

Status of Development

- F16 demonstrated equivalent or better anticancer efficacy than established cancer drugs such as temozolomide in *in vitro* studies with Human glioblastoma U87MG cells.
- In a preclinical study with a mouse intracranial implant model for GBM, F16 administration inhibited tumor growth in 50% of treated animals.
- Results of *in vivo* studies showed F16 to have less secondary toxic effects when compared to currently used chemotherapeutic compounds such as taxol and paclitaxel.

Intellectual Property Status: Provisional patent application filed November 14th, 2019.

Information on Inventors

Dr. Appu Rathinavelu – Dr. Rathinavelu is the Executive Director of the Rumbaugh-Goodwin Institute for Cancer Research at Nova Southeastern University. He is also a Professor of pharmaceutical sciences at NSU's College of Pharmacy.

Dr. Thiagarajan Venkatesan – Dr. Venkatesan is a Associate Research Scientist at NSU's Rumbaugh-Goodwin Institute for Cancer Research.

Dr. Jayanta Das – Dr. Das is a Postdoctoral research scholar at NSU's Rumbaugh-Goodwin Institute for Cancer Research

Mahmood Mansoor S. Algahtani – Mr. Algahtani is a PhD student at NSU College of Pharmaceutical Sciences.

Contact

Gary Margules, Sc.D., Vice President of Research and Technology Transfer
margules@nova.edu

Arunodoy Sur, Ph.D., Technology Licensing Officer
asur@nova.edu • (954) 262-1022

NSU Florida
NOVA SOUTHEASTERN UNIVERSITY

Office of Research and Technology Transfer
3301 College Avenue
Fort Lauderdale, Florida
33314-7796
nova.edu/ott