World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 6, Suppl 2, 2017 ISSN: 2319-5622 USA CODEN: JPROK3

Review Article Full Proceeding Paper

NEW INVESTIGATIONAL DRUG- CANCER SEEKING MISSILE IN BRAIN

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Received on: 05-10-2017; Revised and Accepted on: 08-11-2017

ABSTRACT

A novel drug to treat brain cancer which is notorious for recurring after standard cancer treatment was developed and has been approved as investigational drug by the U.S. Food and Drug Administration. Glioblastoma or malignant glioma is called "Grow and Go" tumors. They make their own blood supply which feeds the tumor cells and make rapid tumor growth. These tumors sends out tentacles that infiltrate deeper into normal brain tissue resulting in the massive brain tumors. A first of a king neural stem cell therapy in combination of common cold virus to seek and attack a lethal and aggressive brain cancer in a Phase 1 clinical trial for patients newly diagnosed with malignant glioma.

KEYWORDS: *Malignant Glioma Treatment, Brain cancer, New Brain Cancer Treatment.*

INTRODUCTION

Glioma is a broad section of brain and spinal cord tumors formed from glial cells that can develop into tumors. The symptoms, diagnosis and treatment depend on different personal factors which differ from patient to patient. These tumors grow large and infiltrate deeper into brain tissues thus infecting the normal brain cells which complicates surgical removal of these tumors. These brain tumors are often diagnosed in lateral stages depending on the type of glioma and low versions of glioma can occur in children too. Males are more slightly susceptible to brain tumors.

Brain tumors such as glioblastoma and anaplastic astrocytoma are currently challenges for neurosurgeons for treatment as well as surgery [1]. Glioma is found in 25-30% of brain tumor patients. In all of the brain tumors malignant glioma particularly relapses very quickly after treatment [2]. Grade IV glioma is very notorious for recurring quickly after surgery and returns to its previous size within 6 months of treatment [3]. Without treatment malignant glioma patients have an average life of 17 weeks and can be prolonged to 30 weeks after treatment. Patients with recurrent glioma repeatedly undergo treatment in short intervals which is severe physical and economical burden for both patient and society [4]. Therefore it is evident that society is in need of a treatment that has low economical burden on patients and can be repeated several times. Malignant gliomas are the most aggressive forms of cancer and are predicted to affect nearly 20,000 new patients this year, according to the American Brain Tumor Association. Sometimes called the "grow-and-go" tumors, gliomas can make their own blood supply, which fuels the tumors' rapid growth and helps them hatch satellite tumors. Each tumor sends out tentacles that infiltrate and dig deep into normal brain tissue, making complete removal of cancerous cells impossible. Any cancerous cells in the brain left over from standard of care can cause the tumor to recur.

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New Approaches to Malignant Glioma Treatment:

Research in California:

The novel method to treat malignant glioma which is very common for recurring after standard treatment was developed by a scientist and has been approved as an investigational drug by the U.S food and Drug Administration. This is the second time Northwestern University has filed an investigational drug as a sponsor. Dr. Maciej Lesniak, the Michael J. Marchese Professor and chair of neurological surgery at Northwestern University Feinberg School of Medicine and a neuro-oncologist at Northwestern Medicine. "If it works in humans, it could be a powerful weapon against brain cancer and an option that our patients are desperate for" [5].

The reason glioma relapses is because a a small population of cancer cells reside deep in the brain tissue and develop resistance to the standard treatments such as chemotherapy and radiation. And there is no significant develop in the brain tumor treatment in the last decade even though the diagnosis or the population of patients affected by this tumor are increasing. It is very imperative that scientists find new methods for the treatment for malignant glioma.

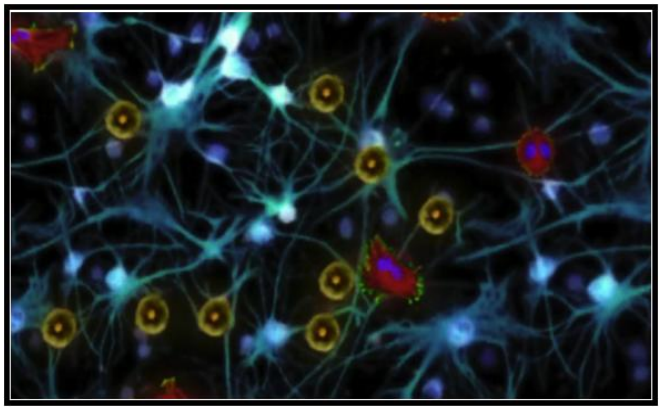

Fig. 1: The image of adenovirus seeking specific target cancer cells

The preclinical work of Dr. Lesniak and his team has shown that the new drug tested at Northwestern University can target this stubborn cancer cells which reside deep in the brain tissue and also can

delay the recurrence of cancer and sometimes even preventing it. The stem cells used in the research came from a collaboration of researchers from City of Hope."We haven't seen significant progress in the last decade for patients with a brain tumor, and that is why it's crucial to do everything we can to find a better treatment for brain tumors," said Dr. Roger Stupp, a co-investigator who is working alongside Lesniak on this clinical trial. "Combining novel therapy with medical expertise, we are able to get one step closer to eradicating this lethal disease" [5]. This investigational drug is packed with neural stem cells to deliver potent virus oncolyotic adenovirus which causes common cold. This adenovirus is genetically engineered to target and kill brain cancer cells. This novel approach on combination with chemotherapy and radiation can enhance the effectiveness of the cancer treatment and may also help in preventing the deadly cancer from recurrence. Dr.Lesniak plans to enroll up to 36 newly diagnosed patients with glioma. These patients will be divided into two groups: those with tumors that can be removed and those where the tumors are not removable by surgery and are supposed to test new drug on these patients.

Research in Spain:

A new approach published in Nature Communications, by a group of researchers from August Pi i Sunyer Biomedical Research Institute, Barcelona Institute of Science and Technology, and Hospital del Mar Medical Research Institute in Spain, shows an novel method to get adenovirus to specifically target cancer cells without attacking healthy cells. These oncolyotic viruses like Newcastle disease viruses infect cancer cells and multiply within the cancer cell which bursts the cell apart otherwise killing the cancer cell. Other virus such as measles viruses are genetically engineered to replicate in cancer cells and some viruses carry chemotherapy drugs to cancer cells. The significance of using viruses in cancer treatment is to specifically find the cancer cells and kill then without harming healthy tissues or cells.

A Novel Process of Using Viruses to Target Cancer Cells:

The new approach focus on set of proteins called cytoplasmic polyadenylation element-binding proteins (CPEBs). These CPEBs control genes involved in production of proteins responsible for maintenance of cells ability to grow, function properly and repair cell damage. Specifically a type of CPEB called CPEB1 is found in almost all normal cells. The control levels of CPEB genes are sometimes disturbed for unknown reasons which results in dysregulation of CPEB1 which in-turn results in the inability of cell damage repairs which leads to cancer cell development. This "dysregulation" results in lower levels of CPEB1 protein in cancer cells and increases in a type of CPEB protein called CPEB4.

When high levels of CPEB4 protein are present in cells, studies have found an increase in tumor growth, increased blood vessel growth to supply blood to the tumor. High levels of CPEB4 protein has been found in pancreatic ductal adenocarcinoma, colorectal cancer, and glioblastoma tumors of the brain. This imbalance in the proteins helps in identifying cancer cells easily by targeting cells low in levels of CPEB1 and high levels of CPEB4.Therefore adenovirus are genetically engineered to target these cells a with high levels of CPEB4 and low CPEB1, so the result is that the virus only attacks the tumor cells and not the healthy cells.The new research proved that targeting modified adenovirus to CPEB4 bearing cells infected the pancreatic cancer cells cultured in the lab and in mouse tumor models and killed the cells by bursting them a part. The viruses found the cells, entered them, multiplied inside them and burst the cancer cells when the viral particles were released, with the potential to infect and kill more cancer cells.

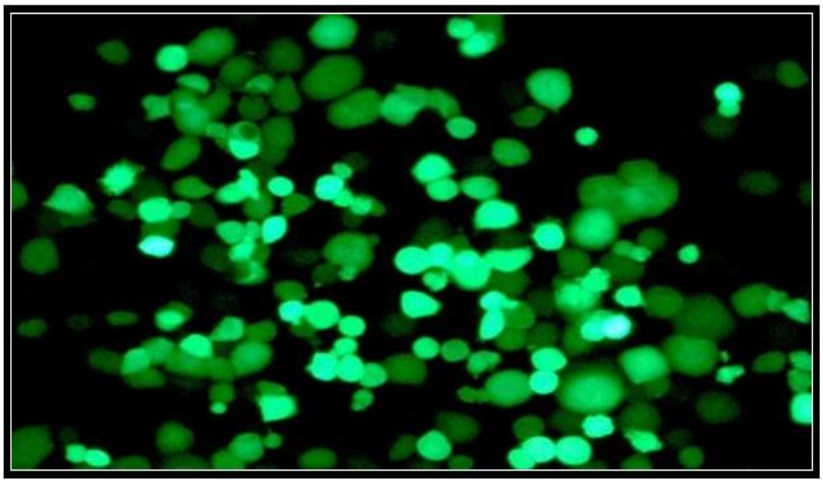

Fig. 2: Tumor cells infeccted by the virus, which expresses a fluorescent protein. Image via IDIBAPS, IRB Barcelona

The benefit of this system doesn't stop there, though. The virus doesn't just make one round of cancer cell killing. It's the therapy that keeps on giving. Newly replicated cells are released when they kill the cancer cells and go on to seek out other CPEB4 cells and kill them as well.This novel approach to targeting viruses to cancer cells can open up more research into ways differences in cancer cell proteins can be targeted for killing by genetically modified viruses."Since CPEB4 is over-expressed in several tumors, this oncoselective strategy may be valid for other solid tumors," said the study authors, suggesting the work has just begun on this promising new treatment [6].

Current Practices to Treat Diffrent Cancers with Virus:

This is not the first time genetically engineered viruses are developed or used in the treatment of cancer. The first genetically engineered oncolyotic live herpes virus treatment was approved by Food and Drug Administration in 2015 for skin cancer called as melanoma treatment. Currently herpes virus is the only approved live virus for cancer treatment. The herpes virus is to be injected into the skin cancer cells for it to work where as adenovirus, the new investigational drug find cancer cells on its own and kills the without affecting healthy cells. Finding the difference between the normal cells and cancer cells is also not new it is vastly used in the genetic tumor markers and has been used in targeting colon and breast cancer chemotherapy. Even though these chemotherapeutic agents are targeting tumor cells these agents are toxic drugs with side effects.
Combination of adenovirus to find cancer cells and genetically engineered to target CPEB4 containing tumor cells and killing them may be the best way for treating cancer without side effects or without harming normal cells. Therefore this treatment may be the perfect solution and worthwhile development from the past decade in eradicating the cancer.

REFERENCES:

1. Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol **2007**;114(2):97–109.[PMC free article] [PubMed]

2. Qaddoumi I, Sultan I, Gajjar A. Outcome and prognostic features in pediatric gliomas: a review of 6212 cases from the Surveillance, Epidemiology, and End Results database. Cancer. **2009**;115(24):5761–5770. [PMC free article] [PubMed]
3. Paugh BS, Qu C, Jones C, et al. Integrated molecular genetic profiling of pediatric high-grade gliomas reveals key differences with the adult disease. J Clin Oncol **2010**;28(18):3061–3068. [PMC free article] [PubMed]
4. Liang ML, Ma J, Ho M, et al. Tyrosine kinase expression in pediatric high grade astrocytoma. J Neurooncol **2008**;87(3):247–253. [PubMed]
5. https://news.northwestern.edu/stories/2017/may/cold-virus-stem-cells-brain-cancer/.
6. https://www.mdanderson.org/publications/conquest/conquest-fall-2015/unleashing-the-cold-virus-to-kill-cancer.html.

How to cite this article:

Bhargavi M. et al. NEW INVESTIGATIONAL DRUG- CANCER SEEKING MISSILE IN BRAIN. J Pharm Res 2017;6(Suppl 2):15-17.

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil