Fighting brain tumors with the help of viruses and molecules

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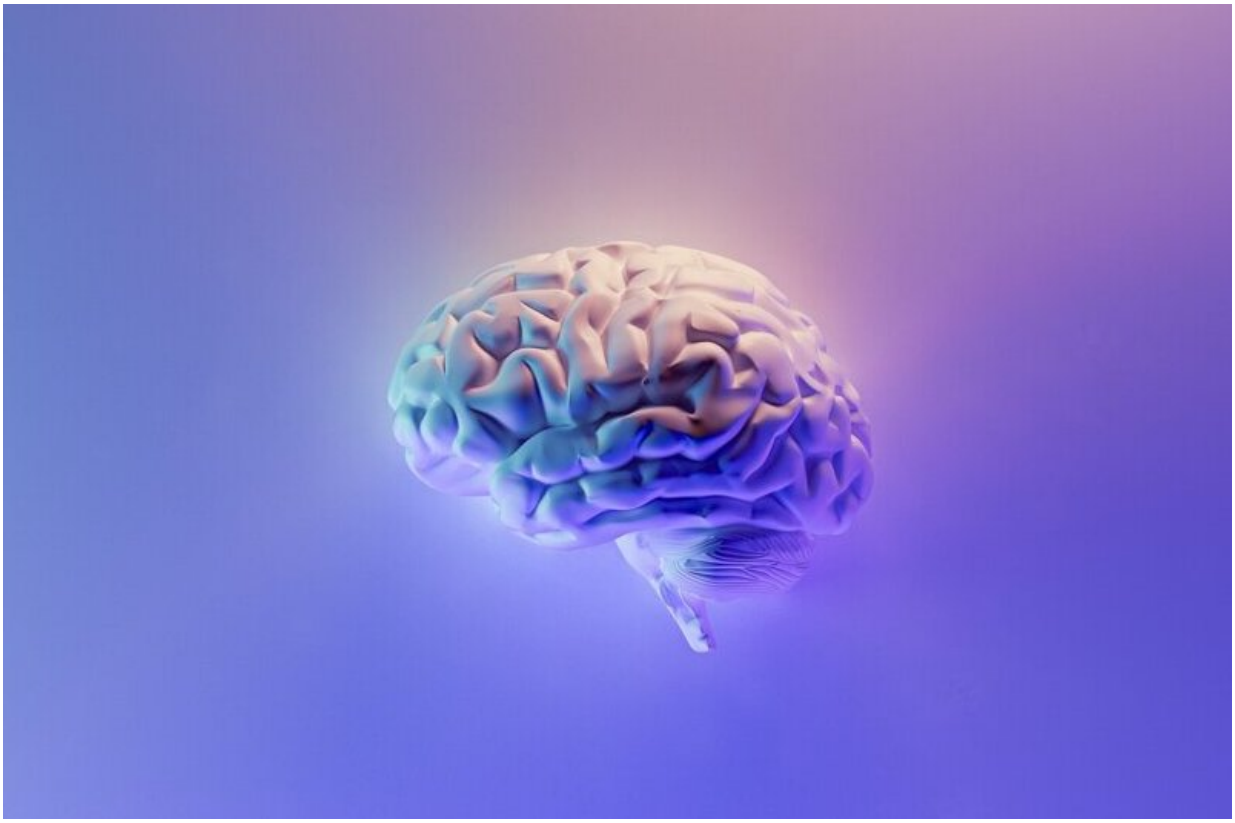

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By harnessing unusual allies, pioneering cancer treatments could reduce the need for invasive surgery and save lives.

Dr. Marta Alonso, a Spanish biomedical researcher, developed an interest in pediatric brain tumors during a traineeship in the US state of Texas.

Alonso had a chance encounter in 2007 at the MD Anderson Cancer Center in Houston with the family of a teenager with medulloblastoma—an untreatable brain tumor that is also the most common type in children. The meeting steered her to an area of the profession with no heart-warming success stories but the potential for important advances.

Career-determining moment

"Talking to this family and understanding the difficulties and the lack of available treatments made me decide that studying pediatric brain tumors was what I wanted to do," said Alonso.

After returning to Spain and setting up her own laboratory in 2010, she began researching cancer treatments in an emerging area called oncolytic virotherapy. This field—counter-intuitively perhaps to non-specialists—involves the use of viruses to treat cancers.

Now Alonso, a faculty member in the Medical Oncology Department of the University of Navarra in Spain, leads a research project to make advances in virus-based treatments for brain tumors.

Called ViroPedTher, the project began in March 2019 and is due to run through August 2024.

For decades, researchers have been trying to improve the prospects for people diagnosed with brain cancer. Most patients—97%—die within five years of diagnosis.

For every 100 000 people in the EU, approximately 11 men and eight women develop brain tumors each year, according to the European Cancer Information System. Over 50,000 Europeans and 250,000 people globally die annually from such cancer.

Immune-system support

There are over 100 types of brain tumors, some more aggressive than others, and survival rates are generally low.

ViroPedTher focuses on two relatively rare types: gliomas and teratoid/rhabdoid tumors.

Both develop deep in the brain and affect children as young as three years. Many of these tumors can't be surgically removed as a result of their position in the brain.

"In some cases, you can use radiotherapy and there are different mixtures of drugs," said Alonso. "But the survival rate is very poor and the quality of life of those who live longer is usually very poor due to the side effects of treatment."

Her approach is to use viruses as a natural ally to help stimulate the immune response of the human body to attack and destroy cancer cells.

She develops modified viruses, designed to trigger specific genetic pathways that encourage immune cells to attack tumor cells more aggressively.

Trial with children

Scientists have long known that, in some cases, viral infections can boost

the immune system and help cancer patients fight off their tumors.

But common viruses may also weaken vulnerable patients and hasten their deaths.

Alonso and her team are trying to create viruses that could deliver the benefits without the risks.

In a clinical trial, the researchers injected a modified adenovirus—one of the many viruses that cause the common cold—into the brain tumors of 12 patients as young as about three years.

The adenovirus was genetically modified to maximize the immune response to the cancer cells. The children gained on average six months of life, living almost 18 more months from a usual period without the treatment of 12 months, according to Alonso.

"We didn't record any significant adverse effects, so we think we are on a right track to find a treatment that could make a difference," she said.

Alonso and her team are fine-tuning the virus to improve its ability to turn the immune system against the tumors. The researchers hope to conduct larger-scale clinical trials as soon as mid-2024.

Glowing brains

Viruses aren't the only potential allies in the fight against brain tumors. Light is too.

This was the focus of a separate research project led by Dr. Theodossis Theodossiou, a senior researcher at the Institute for Cancer Research of Oslo University Hospital in Norway.

Named Lumiblast, the project ran for more than six years until end-January 2023 and has raised hopes of its own breakthrough. In addition to Norway, the researchers came from Greece, Spain and the UK.

The team examined the ability of light-sensitive compounds like protoporphyrin IX—which is naturally produced in human cells—to destroy brain tumors from within and avoid the need for surgery.

The researchers focused on glioblastoma, which accounts for 35% to 40% of all cases of cancerous brain tumors.

Protoporphyrin IX accumulates preferentially in glioblastoma cells. Neurosurgeons currently use its ability to glow when illuminated by light to define the boundaries of tumors during surgery.

When exposed to light, protoporphyrin IX produces oxygen byproducts called "reactive oxygen species" that destroy cancer cells, according to Theodossiou.

These molecules could, in theory, eat the tumor from the inside—if enough light could somehow be provided.

"The problem is that tissue is not easily penetrable by light," said Theodossiou. "The penetration is probably limited to a few millimeters."

As a result, even with open-cranium surgery needed to allow the light to penetrate, it's impossible to reach all parts of the cancer.

Natural chemistry

So the Lumiblast researchers took another route to the same end: they hunted for compounds capable of producing a chemical reaction that would make them glow and thereby activate protoporphyrin IX without

direct exposure to external light.

The process is called chemiluminescence, which also lights up fireflies as well as manufactured objects such as glow sticks, party decorations, kites and emergency lighting.

The compounds could be injected into the patient's blood stream or administered through a drip, according to Theodossiou.

His team tested a handful of promising compounds. Several, as a result of the chemiluminescent reactions, helped destroy cultured glioblastoma cells in the lab as well as in small tumors implanted under the skin of mice.

Research has continued since the project ended and the researchers plan as soon as 2024 to test this method on tumors in animal brains.

Theodossiou believes that initial studies with human patients could start in two to three years.

"We are very optimistic and believe that this approach could offer a cure," he said. "We will be more certain after the next phase of animal experiments."

More information:

- ViroPedTher
- Lumiblast

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