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Editors' notes

New compounds target and kill brain cancer cells after being energized by low X-ray dose

by Nanyang Technological University

Research fellow Dr Huang Jingsheng from NTU Singapore's School of Chemistry, Chemical Engineering and Biotechnology preparing new anti-brain cancer compounds in a fume hood. A silica column was used to get a purified form of the compounds (yellow liquid in flask). Credit: NTU Singapore

Researchers led by Nanyang Technological University, Singapore (NTU Singapore) have developed a new and precise way to treat the most common type of brain cancer using a substantially lower dose of X-rays than existing radiation treatments.

The method has been shown to curb the growth of brain tumors in mice, which paves the way for future clinical applications in humans.

Every year, more than 300,000 people are diagnosed globally with glioblastoma, the most common brain cancer among adults. The cancer starts as a growth of brain cells and, if not treated, quickly spreads through the brain. On average, patients diagnosed with glioblastoma survive for about one-and-a-half years.

One way to treat it is by using radiation like X-rays to kill the cancer cells. However, radiotherapy can accidentally damage healthy cells near the tumor, leading to side effects such as nausea, hair loss and memory problems.

Radiodynamic therapy is a more recent treatment option under development, in which a patient is injected with specially made compounds that create cancer-killing free radicals when X-rays activate them. The dose of X-rays patients receive to activate the compounds is lower, about 20% to 30% of the dose for conventional radiotherapy.

However, the anti-cancer compounds used in radiodynamic therapy, which contain heavy metals, do not target cancer cells accurately. They find their way into healthy cells and can be activated if they are close to where the patient receives the X-rays, leading to damage in the healthy cells.

Now, new research led by NTU's Prof. Pu Kanyi, from the School of Chemistry, Chemical Engineering and Biotechnology, is addressing these problems to make radiation treatment for glioblastoma safer. The study is published in *Nature Materials*.

Precision cancer killing

At the heart of Prof. Pu's advance is a novel compound developed by his team known as a molecular radio afterglow dynamic probe or "MRAP." It comprises biochemicals and iodine and no heavy metals.

In experiments with mice that had brain cancer, the MRAPs were injected directly into the animals' tumors, followed by X-rays at the same location. The X-ray dosage was equivalent to more than six times lower than the amount administered in existing radiodynamic therapy methods.

The MRAPs in the tumors absorb the X-ray radiation and become energized, unleashing cancer-killing free radicals only when they encounter a specific enzyme produced in abnormally large quantities by brain tumor cells.

PhD student Xu Cheng from NTU Singapore's School of Chemistry, Chemical Engineering and Biotechnology checking an X-ray machine for radiation leakage. The properties of new anti-brain cancer compounds were determined by energizing them with X-rays in the machine. Credit: NTU Singapore

In their experiments, the NTU team observed that the MRAPs did not produce free radicals in normal cells, creating no side effects. By contrast, traditional radiodynamic therapy compounds are not as "smart," and their anti-cancer functions can become activated even in healthy cells.

As a result, the side effects of using MRAPs in humans are expected to be lower than other types of radiation treatment.

After treatment with MRAPs, the brain tumors in the mice stopped growing, and these mice survived twice as long as untreated mice—76 days compared with 37.

The animals also showed no sign of tissue damage nor apparent weight loss after being treated with MRAPs. The compounds were eventually passed out through urine and feces.

More information: Jingsheng Huang et al, Molecular radio afterglow probes for cancer radiodynamic theranostics, *Nature Materials* (2023). DOI: 10.1038/s41563-023-01659-1