Light-activated 'photoimmunotherapy' could enhance brain cancer treatment

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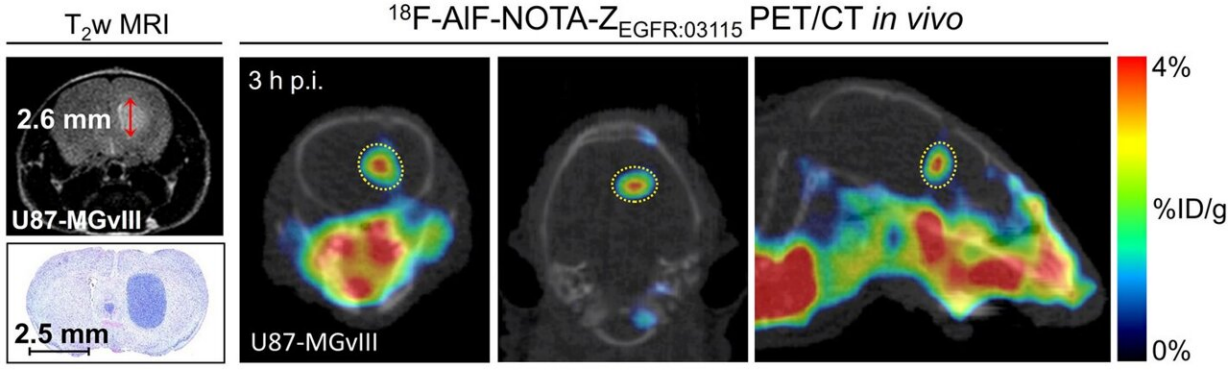
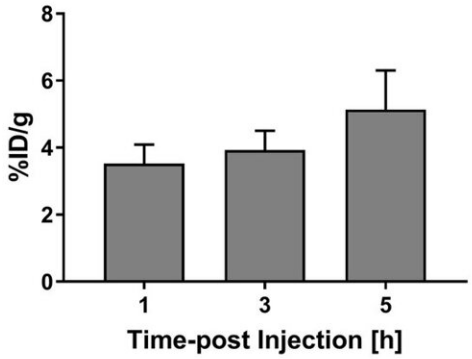
A.

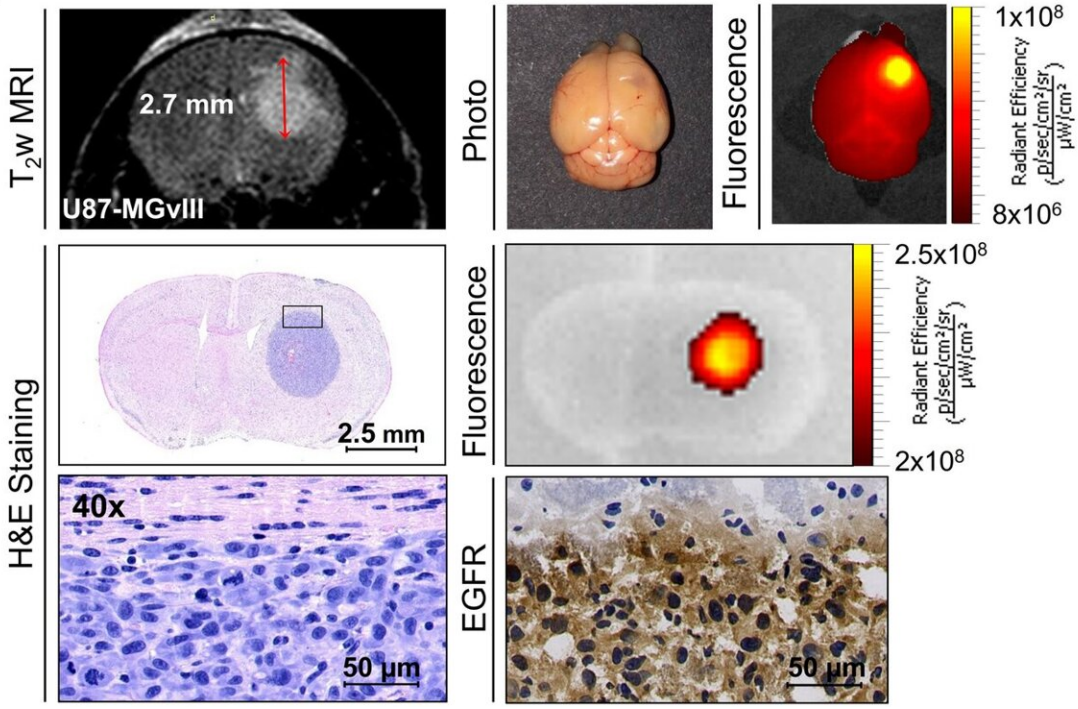


B.



	1 h	3 h	5 h
% ID/g_{max}	3.71 ± 0.64	4.35 ± 0.69	5.64 ± 1.25
% ID/g_{50}	3.52 ± 0.57	3.93 ± 0.58	5.14 ± 1.17

C.



Characterization of the orthotopic U87-MGvIII model. A In vivo axial T2-weighted MRI image and corresponding axial, coronal, and sagittal PET/CT images of the orthotopic U87-MGvIII tumor 3 h post-injection of the ^{18}F-AlF-NOTA-$Z_{EGFR:03115}$ compared to the haematoxylin/eosin staining. B In vivo uptake values 1, 3, and 5 h after i.v. injection of the radiotracer (mean ± SEM), measured as % ID/g_{50} and % ID/g_{max}. C In vivo axial T_2-weighted MRI image and corresponding ex vivo photography and fluorescence image 5 days after tumor cell engraftment (tumor diameter, 2.7 mm). Brain collection and fluorescence imaging were performed 1 h after i.v. injection of 18 μg of $Z_{EGFR:03115}$-IR700. Haematoxylin/eosin staining and near-infrared image of $Z_{EGFR:03115}$-IR700 were performed on the consecutive brain sections. The EGFR immunostaining confirmed the high level of EGFR. Credit: *BMC Medicine* (2022). DOI: 10.1186/s12916-021-02213-z

An innovative light-activated therapy developed at The Institute of Cancer Research, London, could help detect and treat an aggressive brain cancer type, a new study shows.

The "photoimmunotherapy" combines a special fluorescent dye with a cancer-targeting compound, which together boosts the body's immune response.

In studies in mice, the combination was shown to improve the visibility of cancer cells during surgery and, when activated by near-infrared light, to trigger an anti-tumor effect.

The treatment, studied by an international team of researchers from the ICR and the Medical University of Silesia, Poland, could ultimately help surgeons to remove brain cancers like glioblastoma more effectively, and boost the body's response to cancer cells that remain after surgery.

Lighting-up brain cancer

Glioblastoma multiforme, also known as GBM, is one of the most common and aggressive types of brain cancer. New ways to improve surgery could help patients live for longer.

Surgeons often use a technique called Fluorescence Guided Surgery to treat diseases like glioblastoma and other brain cancers, which uses dyes to help identify the tumor mass to be removed during surgery.

But due to these tumors growing in sensitive areas of the brain like the motor cortex, which is involved in the planning and control of voluntary movements, glioblastoma surgery can leave behind residual tumor cells that can be very hard to treat—and which mean the disease can come back more aggressively later.

The new research, published in the journal *BMC Medicine*, builds on Fluorescence Guided Surgery using a novel technique called photoimmunotherapy (PIT).

This treatment uses synthetic molecules called "affibodies"—small proteins engineered in the lab to bind with a specific target with high precision.

In this study, the researchers combined an "affibody" created to recognize a protein called EGFR—which is mutated in many cases of glioblastoma—with a fluorescent molecule called IR700, which is used in surgery.

Shining light on these compounds causes the fluorescent dye to glow, highlighting microscopic regions of tumors left in the brain, while switching to near-infrared light triggers anti-tumor activity that kills tumor cells.

Offering new hope for brain cancer

The researchers tested this combined molecule, or "conjugate"—known scientifically as ZEGFR:03115-IR700—in mice with glioblastoma. They could see the cancer-targeting compound fluorescing in the brain tumors during surgery, just one hour after administration.

Shining near-infrared light on the tumor cells then activated the anti-tumor effect of the compound, killing cancer cells: scans of mice treated with the compound showed distinct signs of tumor cell death compared with untreated mice.

Photoimmunotherapy also triggered immune responses in the body that could prime the immune system to target cancer cells, so the treatment could help prevent glioblastoma cells from coming back after surgery.

As well as being a possible future treatment for glioblastoma, the approach used for ZEGFR:03115-IR700 could also be adapted against other targets in other forms of cancer, using new affibody molecules.

Researchers at the ICR are now also studying the treatment in the childhood cancer neuroblastoma.

Study leader Dr. Gabriela Kramer-Marek, Team Leader in Preclinical Molecular Imaging at the ICR, said: "Brain cancers like glioblastoma can be hard to treat and sadly, there are too few treatment options for patients. Surgery is challenging due to the location of the tumors, and so new ways to see tumor cells to be removed during surgery, and to treat residual cancer cells that remain afterwards, could be of great benefit.

"Our study shows that a novel photoimmunotherapy treatment using a combination of a fluorescent marker, 'affibody' protein and near-infrared light can both identify and treat leftover glioblastoma cells

in mice. In the future, we hope this approach can be used to treat human glioblastoma and potentially other cancers too."

Professor Axel Behrens, Scientific Director of the Cancer Research U.K. Convergence Science Center at the ICR and Imperial College London, and Leader of the Cancer Stem Cell Team at the ICR, said: "Multidisciplinary working is critical to finding innovative solutions to address the challenges we face in cancer research, diagnosis and treatment—and this study is a great example of how researchers at our center are working across traditional discipline boundaries. This research demonstrates a novel approach to identifying and treating glioblastoma cells in the brain using light to turn an immunosuppressive environment into an immune-vulnerable one, and which has exciting potential as a therapy against this aggressive type of brain tumor."

More information: Justyna Mączyńska et al, Triggering anti-GBM immune response with EGFR-mediated photoimmunotherapy, *BMC Medicine* (2022). DOI: 10.1186/s12916-021-02213-z

Provided by Institute of Cancer Research