Fluorescent dyes 'light up' brain cancer cells

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Two new fluorescent dyes attracted to cancer cells may help neurosurgeons more accurately localize and completely resect brain tumors, suggests a study in the February issue of *Neurosurgery*, official journal of the Congress of Neurological Surgeons.

Dr. John S. Kuo and colleagues of University of Wisconsin School of Medicine and Public Health, Madison, evaluated two "tumor-selective" fluorescent agents—called CLR1501 and CLR1502—for their ability to differentiate brain tumors from normal brain tissue in mice. "This study demonstrates the promising potential of CLR1501 and CLR 1502 analogs for use in fluorescence-guided tumor surgery," the researchers conclude.

Green and Near-Infrared Fluorescent Dyes Make Cancer Cells Glow...

CLR1501 and CLR1502 are synthetic analogs of the tumor-targeting agent alkylphosphocholine (APC), which is specifically attracted to cancer cells. The new agents were molecularly altered to carry fluorescent dyes that glow under lights with specific wavelengths—either in the green (CLR1501) or near-infrared (CLR1502) range. Viewed under appropriate conditions, the dyes make tumor cells "light up" so that they can be readily distinguished from neighboring normal brain tissue.

Using different types of imaging technologies, Dr. Kuo and colleagues evaluated the ability of CLR1501 and CLR1502 to detect implanted

(xenograft) tumors in mice. The results were compared with imaging studies performed with a dye called 5-aminolevulinic acid (5-ALA), which glows under blue light. Although 5-ALA is used for fluorescence-guided neurosurgery in Europe, it is not yet approved for routine use in the United States.

The results confirmed that CLR1501 and CLR1502 were attracted to tumor cells, and emitted light of specific wavelengths under appropriate imaging conditions. Both APC analogs provided "excellent fluorescence discrimination of tumor from adjacent normal brain." Tumors could be clearly seen using different types of commercially available imaging systems.

Imaging with CLR1501 green dye showed fluorescence similar to that achieved with currently used 5-ALA dye. With the near-infrared CLR1502 dye, fluorescence was even greater than with 5-ALA. The use of near-infrared fluorescence would offer additional advantages during actual surgery, compared to fluorescence in the visible-light range.

...With Possible Uses in Guiding Brain Cancer Surgery

The findings build on previous cellular-level studies suggesting that APC analogs might be useful in guiding brain cancer surgery. Used during surgery for brain cancer, these fluorescent dyes could help neurosurgeons to locate the tumor and to resect it as completely as possible. Removing all visible areas of cancer (gross total resection) significantly improves survival after brain cancer surgery.

In preliminary studies, near-infrared imaging with CLR1502 successfully localized brain tumors through the intact skin and skull of living mice. In addition to fluorescent-guided neurosurgery, APC analogs might play useful roles in diagnosing brain cancers and in targeting chemotherapy drugs directly to cancer cells.

The researchers acknowledge the "inherent limitations" of their experiments, limited to implanted tumors in animals. Further research will be needed to assess issues related to dye administration, visualization, and timing, as well as the optimal technologies for practical use during surgery. Dr. Kuo and coauthors write, "pcoming clinical trials in human tumors are planned for these promising tumor-selective fluorescence agents."

More information: Click here to read "Fluorescent Cancer-Selective Alkylphosphocholine Analogs for Intraoperative Glioma Detection."

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