Novel imaging agent identifies biomarker for iron-targeted cancer therapies

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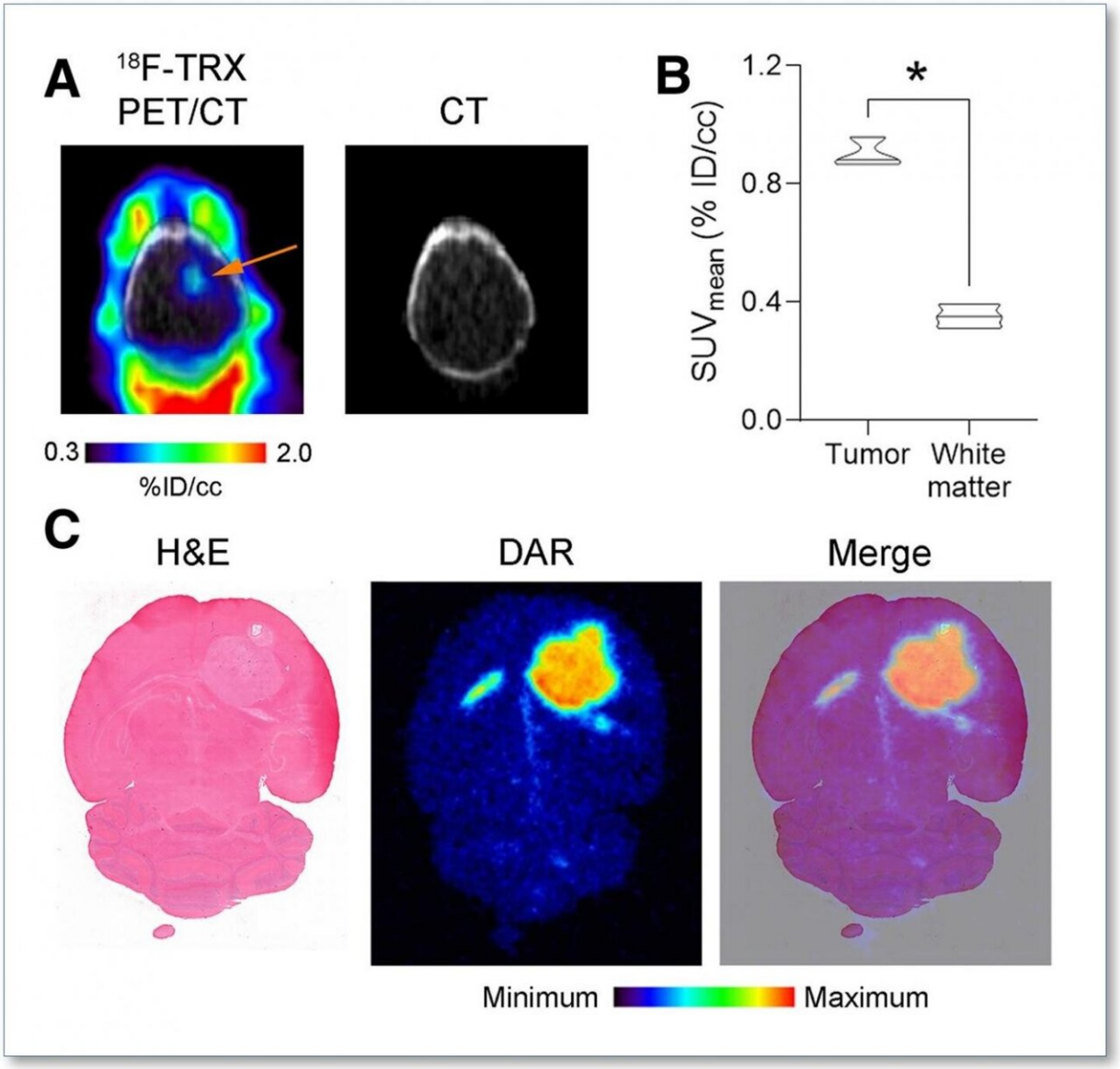

LIP expansion is detectable in an orthotopic glioma model with ^{18}F-TRX. A. ^{18}F-

TRX PET/CT data showing radiotracer uptake in a U87 MG tumor (arrow) implanted within the right hemisphere of a mouse brain. The image was acquired at 90 min post injection. B. Quantification of ^{18}F-TRX uptake using region of interest analysis of the PET data from mice bearing U87 MG tumors (n = 3). The tumor uptake was compared to uninvolved normal white matter on the contralateral region of the brain. C. Digital autoradiography showing the distribution of the radiotracer within a coronal section of the mouse brain. The tissue was stained with H&E and merged with the pseudocolor image of the autoradiography. Credit: Evans, Renslo et al. University of California San Francisco.

A new radiotracer that detects iron in cancer cells has proven effective, opening the door for the advancement of iron-targeted therapies for cancer patients. The radiotracer, ^{18}F-TRX, can be used to measure iron concentration in tumors, which can help predict whether a not the cancer will respond to treatment. This research was published in the July issue of the *Journal of Nuclear Medicine*.

All cancer cells have an insatiable appetite for iron, which provides them the energy they need to multiply. As a result, tumors have higher levels of iron than normal tissues. Recent advances in chemistry have led scientists to take advantage of this altered state, targeting the expanded cytosolic 'labile' iron pool (LIP) of the cancer cell to develop new treatments.

A clear method to measure LIP in tumors must be established to advance clinical trials for LIP-targeted therapies. "LIP levels in patient tumors have never been quantified," noted Adam R. Renslo, Ph.D., professor in the department of pharmaceutical chemistry at the University of California, San Francisco. "Iron rapidly oxidizes once its cellular environment is disrupted, so it can't be quantified reliably from tumor biopsies. A biomarker for LIP could help determine which tumors have

the highest LIP levels and might be especially vulnerable to LIP-targeted therapies."

To explore a solution for this unmet need, researchers imaged 10 tissue graft models of glioma and renal cell carcinoma with ^{18}F-TRX PET to measure LIP. Tumor avidity and sensitivity to the radiotracer were assessed. An animal model study was also conducted to determine effective human dosimetry.

^{18}F-TRX showed a wide range of tumor accumulation, successfully distinguishing LIP levels among tumors and determining those that might be most likely to respond to LIP-targeted therapies. Pretreatment ^{18}F-TRX uptake in tumors was also found to predict sensitivity to therapy. The estimated effective dose for adults was comparable to those of other ^{18}F-based imaging agents.

"Iron dysregulation occurs in many human disorders, including neurodegenerative and cardiovascular diseases, and inflammation," said Michael J. Evans, associate professor in residence in the department of radiology and biomedical imaging at the University of California, San Francisco. "Applying ^{18}F-TRX in the respective patient populations to define the extent of LIP expansion in affected tissues will be an important milestone toward understanding the therapeutic potential of LIP-targeted therapies beyond oncology."

More information: Ning Zhao et al, Ferronostics: Measuring Tumoral Ferrous Iron with PET to Predict Sensitivity to Iron-Targeted Cancer Therapies, *Journal of Nuclear Medicine* (2020). DOI: 10.2967/jnumed.120.252460

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