Docket #: S24-145

Novel Radiopharmaceutical for Non-Invasive Imaging of Ferroptosis in Cancer Therapy

Stanford researchers in Prof. Corinne Beinat's lab have developed a novel radiotracer, [18F]hGTS13, for non-invasive imaging of system xc- activity, enabling the identification of ferroptosis-sensitive cancers and monitoring the efficacy of ferroptosis-inducing therapies. This technology facilitates personalized cancer treatment by assessing drug engagement and predicting therapeutic outcomes.

Ferroptosis, a form of regulated cell death driven by the iron-dependent accumulation of membrane lipid peroxides, has emerged as a promising target for cancer therapy, particularly in glioblastoma multiforme (GBM). However, the current state of the field lacks non-invasive imaging techniques to monitor the engagement of ferroptosis-inducing drugs and to identify patients who would benefit from such therapies. Existing radiotracers, like [18F]FSPG, have limitations in specificity and uptake in inflammatory cells, leading to suboptimal cancer imaging.

The novel radiotracer [18F]hGTS13 specifically targets system xc- to enable non-invasive imaging of ferroptosis in cancer cells. It offers improved radiosynthesis, enhanced specificity for cancer cells over inflammatory cells, and a high tumor-to-brain ratio in glioma models, making it a superior tool for personalized cancer treatment. Evidence from preclinical studies in rats demonstrates its effectiveness in distinguishing ferroptosis-sensitive and resistant cell lines and monitoring drug engagement, highlighting its ability to monitor drug engagement and efficacy in vivo, advancing the current state of cancer therapy.

Figure

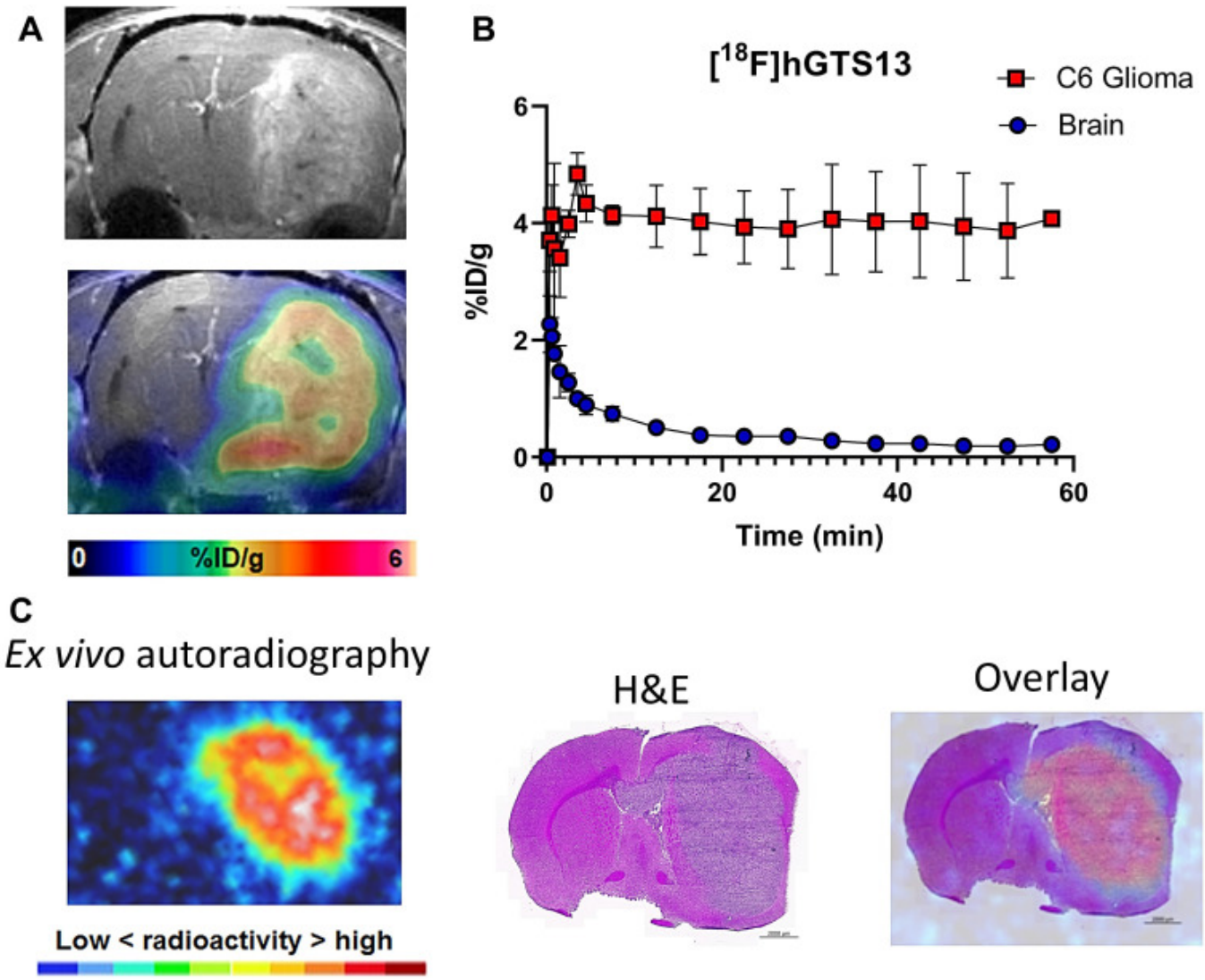

Figure Description: [18F]hGTS13 Uptake in C6 orthotopic glioma-bearing rats. In vivo and ex vivo evaluation of [18F]hGTS13 uptake and retention. (A) Representative [18F]hGTS13 MRI and fused PET/MRI image of orthotopic C6 glioma-bearing rat, summed 30 - 60 min post-injection. (B) Time activity curves of [18F]hGTS13 uptake in C6 glioma and healthy contralateral brain. (C) Ex vivo autoradiography, H&E staining, and corresponding overlay of an excised rat brain bearing an orthotopic C6 glioma following PET/MR imaging. (Image Credit: the Inventors)

Stage of Development

Proof of concept - *in vivo* data in a rat model of glioma

Related Technology
Docket S24-289: Theranostic for Targeted Treatment of Cancers

Applications

- **Novel Imaging Agent:** For Positron Emission Tomography (PET) and Computerized Tomography (CT)
- **Cancer Therapy Monitoring:** Non-invasive imaging to assess the efficacy of ferroptosis-inducing drugs in cancer treatment
- **Drug Engagement Assessment:** Monitors in vivo engagement of system xc- inhibitors, aiding in therapeutic development and optimization

Advantages

- **First-In-Kind** radiotracer to monitor cancer ferroptosis
- **Broad Utility** to monitor various cancers such as primary brain cancers, brain metastases, breast cancer, lung cancer, pancreatic cancer, liver cancer, lymphoma, head and neck cancer, ovarian cancer, or prostate cancer
- **Enhanced Specificity:** [18F]hGTS13 shows reduced uptake in inflammatory cells, improving cancer specificity over [18F]FSPG
- **Improved Radiosynthesis:** Incorporation of a UV-active group facilitates easier radiosynthesis and quality control compared to existing radiotracers

Publications

- Moses, A., Malek, R., et al. (2025). Monitoring of cancer ferroptosis with [18F] hGTS13, a system xc-specific radiotracer. *Theranostics,* 15(3), 836.

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