Docket #: S24-289

Theranostic for Targeted Treatment of Cancers

Stanford researchers in Prof. Corinne Beinat's lab have developed a small molecule radiotheranostic for targeted radionuclide therapy of cancers overexpressing system xc-, such as high-grade glioma and non-small cell lung cancer (NSCLC).

Targeted radionuclide therapy has emerged as a promising approach for cancer treatment, yet numerous cancers still lack safe, effective targeted treatments. The system xc- amino acid antiporter is overexpressed in various cancers, including glioma and NSCLC, and has been identified as a significant target. However, most radiotracers targeting system xc- encounter issues with high uptake in inflammation and undesirable tissue retention, hindering their efficacy and none thus far have been radiolabeled with therapeutic radioisotopes such as bromine-77.

The inventors have developed a second-generation radiotracer targeting system xc- that can be radiolabeled with either fluorine-18 ([18F]hGTS13) for diagnostic imaging or bromine-77 ([77Br]hGTS13) for radionuclide therapy. In pre-clinical studies [18F]hGTS13 showed an improved tumor uptake in NSCLC rat models, and lower pancreas and kidney retention compared to [18F]FSPG, the most widely studied radiotracer targeting system xc-. Dynamic PET/CT imaging results further demonstrate that [18F]hGTS13 has a high and sustained glioma uptake in rats, making it particularly promising for glioblastoma imaging and treatment. In NSCLC in vitro studies, the brominated hGTS13 maintains transporter selectivity for system xc-. Hence, this second-generation hGTS13 radiotracer is a promising small molecule [18F]/[77Br] theranostic pair for high-grade glioma and NSCLC with favorable tumor-targeting properties, biodistribution, and tumor-selective cytotoxicity, and the potential to be applied to multiple other types of cancer.

Stage of Development
Proof of concept: Tested in glioma and NSCLC rat models

Applications

- Cancer theranostics for tumors overexpressing system xc-
    - E.g. High-grade glioma, Non-small cell lung cancer
- Targeted radionuclide therapy (TRT)
- Cancer diagnostic

Advantages

- First-in-class small molecule theranostic radiopharmaceutical for the targeted treatment of cancer
- Favorable pharmacokinetics and biodistribution
- Improved tumor-targeting properties and lower toxicity

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