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FAP-TARGETED DUAL IMAGING FOR GUIDED CANCER SURGERY

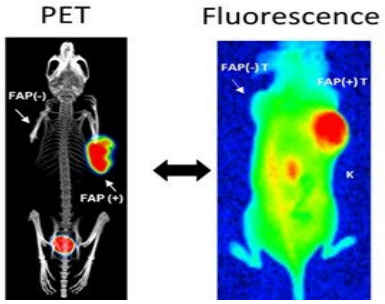
Keywords: PET & fluorescence imaging, dual-modality, Fibroblast activation protein (FAP), near-infrared fluorophore, surgical guidance

INVENTION NOVELTY

The invention presents a new class of zwitterionic, cyanine-based near-infrared (NIR) fluorophores, chemically linked to a scaffold that incorporates two ligands targeting the fibroblast activation protein (FAP). These compounds are distinct due to their sterically shielded zwitterionic architecture, which enhances *in vivo* performance by minimizing nonspecific binding, reducing aggregation, and improving signal-to-background ratios. The modular structure is built around a specific chelating moiety, Fusarinine C, which enables radiolabeling for PET imaging. Selectable FAP binding motifs (e.g. the one featured in FAPI-04 or OncoFAP) and well-defined conjugation units ensure flexible and targeted application across imaging platforms. This unique chemical design optimizes biodistribution and supports both preoperative and intraoperative tumor visualization.

VALUE PROPOSITION

This technology offers a dual-modality molecular imaging platform that combines simultaneously nuclear and optical functionalities with high specificity for FAP-expressing tumors and superior pharmacokinetic properties. Compared to conventional probes, the ones based on sterically shielded zwitterionic fluorophores demonstrate improved hydrophilicity, stability, and reduced background interference, making them ideal for fluorescence-guided surgery. The inclusion of a radiometal chelator supports PET-based diagnostics, enabling seamless integration into clinical workflows from tumor detection to surgical intervention. The approach addresses a critical need for precision imaging tools in oncology, particularly in the context of personalized medicine.



PET/CT and NIR fluorescence imaging of a xenografted mouse injected with the new zwitterionic FFAPi-NIR fluorophore, Source: MUI.

TECHNOLOGY DESCRIPTION

The compounds consist of a trivalent chelator, Fusarinine C, conjugated to a near-infrared (NIR) fluorophore (e.g., s775z or FNIR-Z-759) and to two FAP-targeting moieties (e.g. as the ones based on FAPI-04 or OncoFAP structures). The components are connected via defined linker and conjugation units that allow for chemical flexibility and biological optimization. The invention supports a range of chemical structures and linker variations, enabling tailoring of the imaging agent's properties for specific diagnostic needs. The system is designed for multimodal imaging—offering PET for systemic tumor localization and fluorescence for intraoperative guidance. This combination facilitates pre- and intraoperative tumor delineation, enhances surgical precision and outcomes, and enables potential theranostic applications.

COMMERCIAL OPPORTUNITY

Due to its documented properties (including stability, biodistribution, tumor uptake and tumor retention), the bimodal tracer s775z-FFAPi is a real advance over alternative imaging agents known in the state of the art and can also be applied to a wide range of tumor diseases due to the FAP-targeting vector used. The technology is open for co-development or licensing.

DEVELOPMENT STATUS

FAP specificity and prolonged binding was demonstrated via both radioactive and fluorescence signal *in vitro, ex vivo* and *in vivo* models. The compound s775z-FFAPi showed optimal tumor accumulation, rapid off-target clearance, and strong in vivo stability indicating it as a *best-in-class* candidate for preoperative PET imaging and intraoperative fluorescence-guided surgery of FAP-positive tumors. The compound is currently under investigation in feline patients with FAP-expressing tumors.

PATENT SITUATION

A priority EP patent application has been filed end of March 2025.

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