Award ID:
RP180812

Project Title:
Fluorescently Labeled Somatostatin Analogs for Image-Guided Surgery in Neuroendocrine Tumors

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Health Science Center at Houston

Lay Summary:

Cancer surgery is the foundation for curative therapy and has major therapeutic implications for patients with neuroendocrine tumors (NETs). Unlike most cancers, surgery is performed in NETs even if metastases are present in order to control excessive hormone production that could further stimulate tumor growth. In NETs, surgery is often complicated by difficulties in identifying small liver metastases, which give rise to remarkably high recurrence rates. Accordingly, the goal of this project is to develop a contrast agent that improves intraoperative detection of NETs and increases overall survival. Radiolabeled peptides are widely used in the clinic for NET imaging before and after surgery, but are not suitable for intraoperative use. Thus, surgeons rely on visual inspection and palpation, which are often ineffective for detecting small lesions. We have previously shown that a radiolabeled somatostatin analog, TOC, can be attached to a fluorescent dye and maintain specific targeting to cancer cells that express the somatostatin receptor subtype-2 (SSTR2). We discovered that drug design was critical for maintaining tumor targeting, and identified an innovative chemistry scaffold, known as multimodality chelator (MMC), to add a fluorescent tag to radiolabeled-TOC. Our findings provided the first evidence that a multimodal TOC analog could be used for fluorescence-guided surgery (FGS), and led to the hypothesis of this proposal that optimization of the targeting moiety and dye could produce an intraoperative imaging agent with higher detection sensitivity for residual and micrometastatic disease than our initial agent. This research could have a broad impact on cancer survivorship by equipping surgeons with real-time intraoperative imaging capabilities. Validation of the proposed agent would address significant challenges associated with NET surgery, and serve as a model for other targeted agents suitable for surgical guidance.