CHERENKOV-MEDIATED EXCITATION OF DISCRETE EUROPIUM PROBES FOR IN VIVO LUMINESCENCE IMAGING FOR INTRAOPERATIVE TUMOR RESECTION

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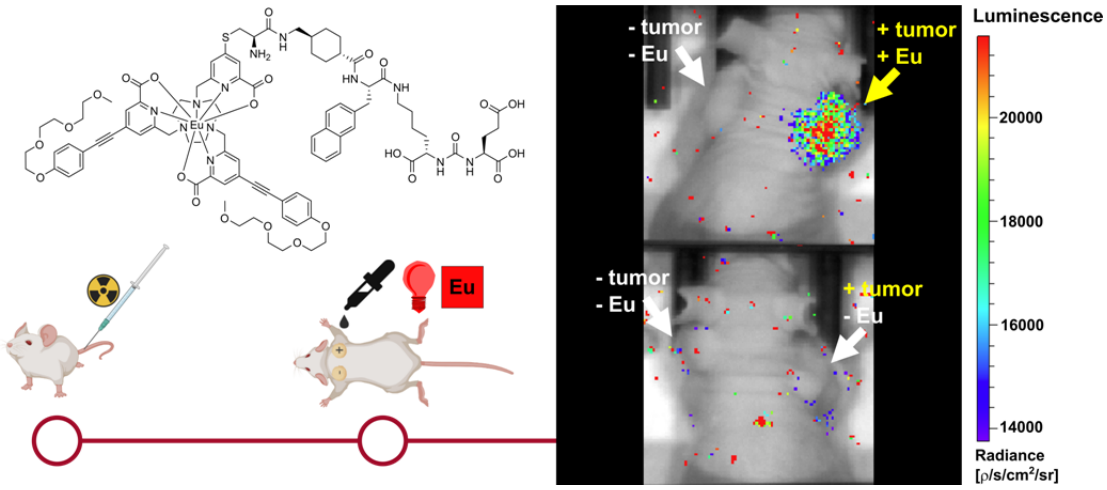
Surgical management of cancers constitutes an essential component of disease management and therapeutic intervention; however, distinguishing between cancer tissue and healthy tissue can be challenging during resection. To this end, fluorescence guided cancer surgery has emerged as a tool to delineate tumor resection margins.[1-2] An alternative to conventional organic fluorophores are lanthanide based luminescence probes, which express long luminescence lifetimes, diminished photobleaching, and produce well defined, narrow emission bands. Previously, we have demonstrated that a discrete, targeted Eu probe can be used in concert with in situ excitation using Cherenkov radiation produced by the positron emitting radionuclide ^{18}F for *in vivo* luminescence imaging.[3] This probe however exhibited limited brightness and affinity to the target.

In this work, we present a next generation Eu based probe [Eu(tcn-pic-PEPA-PEG$_2$)] for *in vivo* luminescence imaging with high quantum yield, identifying a limit of detection comparable to that of organic chromophores (1 nmol) in the presence of 10 µCi of ^{68}Ga as the photon source. The corresponding targeted probe [Eu(tcn-pic-PEPA-PEG$_2$)PSMA] exhibits selective binding to the prostate cancer specific membrane antigen target in vitro. Systemic administration of the targeted PET imaging agent ^{68}Ga-PSMA-617, followed by intratumoral injection or topical application of 10-20 nmol [Eu(tcn-pic-PEPA-PEG$_2$)PSMA] results in a strong and persistent luminescence signal from the target tumor. Successful surgical resection of the affected tissue was demonstrated, and luminescence signal persisted to enable histological imaging.



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