Novel Fluorogenic Probes for Intraoperative Rapid Imaging of Tiny Tumors

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We have succeeded to develop novel fluorogenic probes for various aminopeptidases based on our newly established rational design strategy with intramolecular spirocyclization(1). For example, gGlu-HMRG, a novel fluorogenic probe for gamma-glutamyltranspeptidase (GGT), which is well-known to be upregulated in various cancer cells, was developed. In mouse models of disseminated human peritoneal ovarian cancer, activation of gGlu-HMRG occurred within 1 min of topically spraying onto tissue surfaces that are suspected of harboring tumors, with high tumor-to-background contrast (2). We also proved that tumor regions in real clinical specimen of breast cancer patients, even those smaller than 1 mm in size, could be easily discriminated from normal mammary gland tissues within 1-15 min after probe application(3,4).

Encouraged by these promising results, we prepared a library of fluorogenic probes composed of more than 300 probes for various aminopeptidases. These probes were applied on fresh biopsy samples from esophageal cancer patients, and we found the enzymatic activity of dipeptidyl peptidase-4 (DPPIV) was upregulated in tumor-positive biopsy samples, but not with tumor-negative biopsy samples. Indeed, cancer region in the resected human fresh specimens was clearly visualized by topically spraying DPPIV-activatable fluorescence probes within 10 min(5). These findings clearly demonstrated that our fluorogenic probes should be a breakthrough in rapid detection of tumors during endoscopic and surgical procedures.

References

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