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Imaging

Major finding: A topically applied, cancer cell–specific fluorescent probe visualizes ovarian tumors.

Concept: GGT on the surface of cancer cells rapidly activates the gGlu-HMRG probe.

Impact: The gGlu-HMRG probe can visualize cancer cells during surgical and endoscopic procedures.

A RAPIDLY ACTIVATABLE, TUMOR-SPECIFIC FLUORESCENT PROBE

The success of oncologic surgery depends on direct visualization and complete resection of both bulk tumor and local metastases. However, infiltrative tumor borders and tiny metastases may be difficult to discern with an unaided eye. Although rhe development of cancer-specific, fluorescent imaging probes has enhanced optically guided surgical and endoscopic procedures, existing antibody-based and enzyme-activatable probes can be slow to fluoresce and may require i.v. administration. Urano and colleagues developed a fluorescence-imaging probe that can be topically sprayed onto tumors and is rapidly activated by γ-glutamyltranspeptidase (GGT), a cell membrane–associated enzyme that is overexpressed in cervical and ovarian cancers. In its applied form, the γ-glutamyl hydroxyl methyl rhodamine green (gGlu-HMRG) probe is inactive and hydrophilic. GGT on the surface of cancer cells hydrolyzes the probe, freeing the hydrophobic and highly fluorescent HMRG, which enters cancer cells and accumulates in lysosomes. In this study, the probe was specifically activated by GGT-expressing ovarian cancer cells both *in vitro* and *in vivo*. Remarkably, when the probe was sprayed into the abdominal cavity of mice modeling invasive human ovarian cancer, tumor implants as small as 1 mm were visualized in as short a time as 10 seconds and remained fluorescent for at least 1 hour. With fluorescence-guided laparoscopy, the tumors were effectively removed. The advantages of the gGlu-HMRG probe include its specificity, topical application, and rapidity of activation. Although use of the probe is limited to cancers that express GGT, its design could be applied to target additional cancer-specific cell surface enzymes.

Urano Y, Sakabe M, Kosaka N, Ogawa M, Mitsunaga M, Asanuma D, et al. Rapid cancer detection by topically spraying a γ-glutamyltranspeptidase–activated fluorescent probe. Sci Transl Med 2011;3:110ra119.

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CANCER DISCOVERY

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