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Near-infrared optical imaging of protease activity for tumor detection.

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Abstract

PURPOSE: To build and test an optical imaging system that is sensitive to near-infrared fluorescent molecular probes activated by specific enzymes in tumor tissues in mice.

MATERIALS AND METHODS: The imaging system consisted of a source that delivered 610-650-nm excitation light within a lighttight chamber, a 700-nm longpass filter for selecting near-infrared fluorescence emission photons from tissues, and a charge-coupled device (CCD) for recording images. The molecular probe was a biocompatible autoquenched near-infrared fluorescent compound that was activated by tumor-associated proteases for cathepsins B and H. Imaging experiments were performed 0-72 hours after intravenous injection of the probe in nude mice that bore human breast carcinoma (BT-20).

RESULTS: The imaging system had a maximal spatial resolution of 60 microns, with a field of view of 14 cm2. The detection threshold of the nonquenched near-infrared fluorescent dye was subpicomolar in the imaging phantom experiments. In tissue, 250 pmol of fluorochrome was easily detected during the 10-second image acquisition. After intravenous injection of the probe into the tumor-bearing animals, tumors as small as 1 mm became detectable because of tumor-associated enzymatic activation of the quenched compound.

CONCLUSION: Tumor proteases can be used as molecular targets, allowing visualization of millimeter-sized tumors. The development of this technology, probe design, and optical imaging systems hold promise for molecular imaging, cancer detection, and evaluation of treatment.

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