Near-Infrared Fluorescence Imaging and Quantification of Anti-Angiogenic Therapy using an αvβ3, Integrin-Targeted Agent

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1 PerkinElmer Inc., 2 Merck Research Laboratories, West Point, PA

1 Abstract

Integrins are versatile cell-surface receptors which mediate signal transduction, cell-to-cell interaction and cell-to-extracellular matrix adhesion. These processes lead to cell migration, invasion and extravasation, all key components in angiogenesis, tumorgenesis, and metastasis. Integrins have thus been blamed as critical relevant biomarkers of pathological conditions such as inflammation and tumor progression. Integrin αvβ3 is significantly upregulated in tumor cells and activated endothelial cells during angiogenesis, but not in quiescent endothelium. The aim of this study was to non-invasively image and quantify, using a specific, targeted near-infrared (NIR) fluorochrome agent, Integrine®® 680 (PerkinElmer®) and fluorescence molecular tomography (FMT) imaging, the amount of αvβ3 integrins in human colon tumors. Two tumor xenograft models were used for this purpose. First, using a low molecular weight peptide-conjugated fluorochrome coupled to AE680 dye, we assessed αvβ3 integrin expression levels in human colon tumors in nude mice. Images were reconstructed using the FMT software and the total amount of fluorescence (pmol) was quantified in specific 3D regions of interest around each tumor. A strong correlation was seen between tumor volume and IntegriSense signal (r = 0.68). Images were reconstructed and the total amount of fluorescence was determined in specific 3D regions of interest around each tumor. A strong correlation was seen between tumor volume and IntegriSense signal (r = 0.68).

4 Integrin-Targeted Agent Specifically Detects Integrins in a Mouse Breast Cancer Model

Nu42 mouse were injected subcutaneously bilaterally in the mammary fat pads with mouse breast cancer 4T1 cells, twice weekly. The Anti-Angiogenic Treatment: An Integrin-Targeted Imaging Agent can be Used to Assess Therapeutic Efficacy in a Tumor Xenograft Model

In Vivo Pharmacokinetic and Biodistribution Profile

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