Cy7-Tyr-D-Glu-Cys-Hyp-Tyr(3-Cl)-Gly-Leu-Cys-Tyr-Ile-Gln-NH_2

Cy7-FTP11

Kam Leung, PhD[1]

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Chemical name:	Cy7-Tyr-D-Glu-Cys-Hyp-Tyr(3-Cl)-Gly-Leu-Cys-Tyr-Ile-Gln-NH_2	
Abbreviated name:	Cy7-FTP11	
Synonym:		
Agent category:	Peptide	
Target:	Fibrin	
Target category:	Acceptor	
Method of detection:	Near-infrared (NIR) fluorescence imaging, optical	
Source of signal/contrast:	Cy7	
Activation:	No	
Studies:	• *In vitro* • Rodents	No structure is available in PubChem.

Background

[PubMed]

Optical fluorescence imaging is increasingly used to monitor biological functions of specific targets in small animals (1-4). However, the intrinsic fluorescence of biomolecules poses a problem when fluorophores that absorb visible light (350–650 nm) are used. Near-infrared (NIR) fluorescence (650–1,000 nm) detection avoids the natural background fluorescence interference of biomolecules, providing a high contrast between target and background tissues in small animals. NIR fluorophores have a wider dynamic range and

[1] National for Biotechnology Information, NLM, NIH, Bethesda, MD; Email: MICAD@ncbi.nlm.nih.gov.

Corresponding author.

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minimal background fluorescence as a result of reduced scattering compared with visible fluorescence detection. NIR fluorophores also have high sensitivity, attributable to low background fluorescence, and high extinction coefficients, which provide high quantum yields. The NIR region is also compatible with solid-state optical components, such as diode lasers and silicon detectors. NIR fluorescence imaging is a noninvasive alternative to radionuclide imaging in small animals (4, 5).

Extracellular matrix adhesion molecules consist of a complex network of fibronectins, collagens, chondroitins, laminins, glycoproteins, heparin sulfate, tenascins, and proteoglycans that surround connective tissue cells, and they are mainly secreted by fibroblasts, chondroblasts, and osteoblasts (6). Cell substrate adhesion molecules are considered essential regulators of cell migration, differentiation, and tissue integrity and remodeling. These molecules play a role in inflammation and atherogenesis, but they also participate in the process of invasion and metastasis of malignant cells in the host tissue (7). A meshwork of clotted plasma protein was present in the tumor stroma but not in normal tissues, providing a functional matrix for angiogenesis, cell migration, and tumor cell invasion (8). There are high levels of collagens, fibronectin, and fibrin in the tumor connective tissues.

Thrombosis plays a major role in many cardiovascular diseases such as myocardial infarction, pulmonary embolism, deep venous thrombosis, and cerebral venous thrombosis (9). Thrombosis occurs by an activation process of thrombin (F2 coagulation factor II), which then converts fibrinogen into fibrin. Thrombin initiates the cross-linking of the polymerized fibrin *via* the activation of a transglutamase enzyme called coagulation factor XIII (FXIIIa indicates activated factor XIII) (10). Atherosclerotic lesions often contain microthrombi and fibrin on their surface. Fibrin is associated with a variety of malignant tumors. Fibrin is essential for stroma formation in the tumor with deposition of fibrin, which leads to tumor angiogenesis and metastasis. Hara et al. (11) prepared Cy7-Tyr-D-Glu-Cys-Hyp-Tyr(3-Cl)-Gly-Leu-Cys-Tyr-Ile-Gln-NH_2 (Cy7-FTP11) for use with NIR fluorescence imaging of fibrin in thrombi in mice using high-resolution intravital fluorescence microscopy and fluorescence molecular tomography.

Related Resource Links:

- Chapters in MICAD (fibrin)
- Gene information in NCBI (fibrinogen, fibronectin)
- Articles in Online Mendelian Inheritance in Man (OMIM) (fibrinogen, fibronectin)

Synthesis

[PubMed]

FTP11 was synthesized with solid-phase peptide synthesis (11). Cy7 was conjugated to the N-terminal amino group of FTP11 with addition of Cy7-succinimidyl ester. Cy7-FTP11 was isolated with high-performance liquid chromatography and cyclized by oxidation in

dimethyl sulfoxide with >98% purity. Cy7-FTP11 exhibited an expected molecular mass of 2.62 kDa using matrix-assisted laser desorption/ionization mass spectrometry.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

In vitro fluorescence reflective imaging studies showed that Cy7-FTP11 exhibited significantly higher ($P < 0.0001$) target/background ratios (TBR) than free Cy7 to fibrin in human plasma clots, with TBRs of 6.30 ± 0.34 and 1.20 ± 0.03 (11), respectively. Excess unlabeled FTP11 (100-fold) inhibited the TBR of Cy7-FTP11 to 2.50 ± 0.34 ($P < 0.05$).

Animal Studies

Rodents

[PubMed]

Intravital fluorescence microscopy imaging studies were performed in mice ($n = 5$/group) with the femoral vein exposed and treated with 7.5% $FeCl_3$ solution to induce acute (2 h) and sub-acute (72 h) thrombosis (11). Cy7 or Cy7-FTP11 (150 nmol/kg) was injected *via* retro-orbital administration. NIR fluorescence signal (TBRs) increased in both acute (3.5 ± 0.3) and sub-acute (2.7 ± 05) thrombi at 60 min after injection of Cy7-FTP11, whereas no increase was observed with Cy7 (0.46 ± 0.08). Blocking studies were performed in mice ($n = 4$/group) with acute thrombosis after pretreatment with 100-fold excess unlabeled FTP11 (1,500 nmol/kg) 30 min before Cy7-FTP11 (15 nmol/kg) injection. Thrombus TBR at 60 min decreased from 1.60 ± 0.11 to 0.99 ± 0.04 ($P < 0.01$). Histostaining of the veins confirmed the localization of NIR fluorescence signals in the thrombi. Cy7-FTP11 exhibited a blood half-life of 2.82 min ($n = 5$).

Noninvasive fluorescence molecular tomography imaging studies were performed in mice with the left jugular vein treated with 7.5% $FeCl_3$ solution to induce sub-acute thrombosis (11). The contralateral right jugular vein was sham-operated. FMT signals from jugular veins were co-registered with anatomic computed tomography images. The TBR of the left jugular vein thrombi (3.5 ± 0.7) was 1.3-fold higher than that of the contralateral right jugular vein (1.5 ± 0.3) ($P < 0.05$). *Ex vivo* NIR fluorescence signals were 3.9 ± 0.4 and 2.4 ± 0.4 ($P < 0.05$) for the left and right jugular veins, respectively.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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