Supplementary Material and Methods

***In vitro* activation of PEG-peptide-TMR is dependant on soluble MMPs**

1 x 10^5 HT1080 cells were seeded in DMEM medium containing 10% serum in a 24-well plate at 37°C in a CO_2 incubator overnight. The cells were cultured in serum-free DMEM medium for 48 h and then stained with 5 µM PEG-peptide-TMR in the presence or absence of 50 µg/ml TIMP1 or 50 µg/ml TIMP2 (AnaSpec, San Jose, CA, USA) at 37°C for 1 h. After washing with PBS, the fluorescence of viable cells was observed under a fluorescence microscope (Axiovert 200, Carl Zeiss MicroImaging, GmbH, Germany).

***In vivo* micro-PET imaging of the kidney**

BALB/c nude mice (*n* = 3) bearing established HT1080 and MCF-7 tumors (100–200 mm^3) in their right and left hind leg, respectively, were anesthetized by halothane vapor with a vaporizer system and then were intravenously injected with 3700 kBq (in 100 µL) PEG-peptide-^{18}F-TMR. PET imaging was sequentially performed at 15, 60, and 120 min. The tumor-bearing mice were positioned in a micro-PET scanner (R4; Concorde Microsystems, Knoxville, Tenn) with their long axis parallel to the transaxial plane of the scanner. The scanner has a computer-controlled bed with a 10.8-cm transaxial and 8-cm axial field of view. It has no septa and operates exclusively in a three-dimensional list mode. All raw data were first sorted into three-dimensional sinograms, followed by Fourier rebinning and ordered-subsets expectation maximization image reconstruction. Fully three-dimensional list-mode data were collected by using an energy window of 350–750 keV and a time window of 6 nsec. Image pixel size was 0.85 mm transaxially, with a 1.21-mm section thickness. The region of interest was

analyzed with ASIPro VM™ version 5.0 (Concorde Microsystems, Knoxville, TN, USA.) analysis software.

Biodistribution of PEG-peptide-^{18}F-TMR

Tumor-bearing female BALB/c nude mice (n=3) were intravenously injected with 3700 kBq (in 100 µL) PEG-peptide-^{18}F-TMR. Animals were killed after anesthesia with pentobarbital (65 mg/kg) at 15, 60, and 120 min. Radioactivity in isolated tumors and tissues was measured with a multichannel gamma-counter. The biodistribution of the probe was expressed as percent injected dose per gram of tissue (%ID/g).

Supplementary Figure legends

Supplementary Figure 1. *In vitro* activation of PEG-peptide-TMR is dependant on soluble MMPs. HT1080 cells were incubated with 5 μM PEG-peptide-TMR in the presence or absence of TIMP-1 or TIMP-2 at 37^{o}C for 1 h. Cell-bound fluorescence of viable cells was analyzed by flow cytometry.

Supplementary Figure 2. In vivo Micro-PET imaging of kidney. Mice bearing established HT1080 (left hind legs) and MCF-7 (right hind legs) tumors were injected with 3700 kBq PEG-peptide-^{18}F-TMR. Coronal and transverse images were acquired at 15, 60 and 120 min after injection. Coronal images of kidney section were acquired at 15, 60 and 120 min after injection of the probe.

Supplementary Figure 3. Biodistribution of PEG-peptide-^{18}F-TMR**.** Mice bearing established HT1080 and MCF-7 tumors were injected with 3700 kBq of PEG-peptide-^{18}F-TMR. Selected organs and tumors were removed from the mice after 15 (black column), 60 (white column) and 120 (gray column) min. The radioactivity of individual organs was measured in a γ-counter and normalized for sample weights. The biodistribution of PEG-peptide-^{18}F-TMR in selected organs was expressed as % injected dose/g tissue. Data represent mean± SEM.