ONLINE METHODS

Full experimental details are presented in the supplementary information.

Chemistry and radiochemistry. Protein functionalization with DFO and subsequent radiolabeling with ^{89}Zr was accomplished in accordance with previously reported methods[19,39]. Zirconium-89 was produced *via* the ^{89}Y(*p*,*n*)^{89}Zr transmutation reaction on an EBCO TR19/9 variable beam energy cyclotron (Ebco Industries Inc.) and isolated in high radionuclidic and radiochemical purity (RCP) >99.9%, with an effective specific-activity of 195–497 MBq μg^{-1}, (5.28–13.43 mCi μg^{-1}) as ^{89}Zr-oxalate[17]. Quantification of radioactivity was achieved using a calibrated Automatic Wizard^2 Gamma Counter (Perkin Elmer) employing a dynamic energy window of 800–1000 keV for ^{89}Zr (909 keV emission). Appropriate decay correction was employed throughout.

Stability and metabolism studies. Radiotracer stability was assessed *in vitro* by incubation in solutions of saline and PBS for 5 days at 37 ºC. RCP was determined by radio-ITLC and γ-counting, and the protein-labeled fraction was measured at various time points by size-exclusion chromatography (PD-10, Sephadex G-25M, GE Healthcare). We conducted *in vitro* and *in vivo* metabolism studies in mouse urine, and mouse and human blood by using size-exclusion, radiometric, high-performance liquid chromatography (radio-HPLC). The radio-HPLC system was equipped with a Tosoh Science G3000SWXL column (300 mm × 7.8 mm; 5 μm; Fisher Scientific), and eluted with a 0.02 M sodium acetate, 0.15 M sodium chloride, pH6.4 mobile phase at flow rate of 1 mL min^{-1} at ambient temperature.

***In vivo* models.** All animal experiments were conducted in compliance with protocols approved by the Institutional Animal Care and Use Committee (IACUC) of Memorial Sloan-Kettering Cancer Center. Genetically engineered mouse (GEM) models of human prostate cancer (Hi-Myc mice at 4 and 12 months old) used in these experiments were maintained in our animal housing facility. Mouse models of inflammation were developed by s.c. injection of turpentine oil (50 μl, neat) on the right hind limb of intact, immunocompetent male FVB mice (Taconic Farms Inc.). Xenograft models were induced on the right flank by sub-cutaneous (s.c.) injection of 2.0×10^5 MycCaP cells in a 200 μl cell suspension of a 1:1 v/v mixture of media with reconstituted basement membrane (BD Matrigel™, Collaborative Biomedical Products Inc.). Palpable MycCap tumors (50–250 mm^3) developed after a period of 14–21 days. Surgical castration was performed under anesthesia in accordance with our IACUC approved protocol.

Biodistribution studies. Biodistribution studies were conducted in accordance with previously reported methods[19].

Small-animal PET imaging. PET imaging experiments were conducted on a microPET Focus 120 scanner (Concorde Microsystems). In repeated studies (n = 4), mice were administered formulations of ^{89}Zr-mTf (11.6–13.7 MBq, [313–370 μCi], 35–41 μg of protein, in 200 μl sterile saline for injection) *via* i.v. tail-vein injection. Approximately 5 minutes prior to recording PET images, mice were anesthetized by inhalation of 1–2% isoflurane (Baxter Healthcare) in an oxygen gas mixture and placed on the scanner bed. PET images were recorded at various time-points between 1 – 120 h post-injection. Image reconstruction and processing details have been reported elsewhere[19]. Manually drawn 2-dimensional regions-of-interest (ROIs) or 3-

dimensional volumes-of-interest (VOIs) were used to determined the maximum and mean radiotracer accumulation in units of %ID g^{-1} (decay corrected to the time of injection) in various tissues. Images were analyzed by using ASIPro VM^{TM} software (Concorde Microsystems).

Co-registered PET/CT. Computed tomography (CT) images were acquired on a small-animal Siemens/CTI microCAT II (Siemens Medical Solutions) scanner with an 8.5 cm axial by 5.0 cm transaxial field-of-view. Co-registered PET/CT images were recorded at 16 h post-radiotracer administration. Images from the two separate modalities were mapped to a matrix and co-registered in accordance with previously reported methods[40].

Magnetic resonance (MR) imaging. Mouse prostate MR images were acquired on a Bruker 4.7T Biospec scanner operating at 200 MHz and equipped with a 400 mT m^{-1} ID 12 cm gradient coil (Bruker Biospin MRI).

Statistical analyses. Data were analysed by using the unpaired, two-tailed Student's *t*-test. Differences at the 95% confidence level ($P<0.05$) were considered to be statistically significant.