Supporting Information

PSMA-Targeted Theranostic Nanocarrier for Prostate Cancer

Orielyz Flores[1,2] Santimukul Santra,[1] Charalambos Kaittanis,[3] Rania Bassiouni,[2]
Amr S Khaled,[4] Annette R. Khaled,[2] Jan Grimm,[3] and J Manuel Perez[5]*

1) Nanoscience Technology Center and Chemistry Department,
University of Central Florida,
Orlando FL, 32827

2) Burnett School of Biomedical Science, College of Medicine,
University of Central Florida
Orlando FL, 32827

3) Molecular Pharmacology Program and Department of Radiology
Memorial Sloan Kettering Cancer Center,
New York, NY., 10065

4) Orlando VA Medical Center
Orlando, FL 32827

5) Biomedical Imaging Research Institute, & Samuel Oschin Comprehensive Cancer Institute
Department of Biomedical Sciences and Department of Neurosurgery
Cedar Sinai Medical Center,
Los Angeles CA, 90048

* Corresponding Author
J Manuel Perez, PhD
Professor
Department of Biomedical Sciences & Department of Neurosurgery
Biomedical Imaging Research Institute & Samuel Oschin Comprehensive Cancer Institute
Cedar Sinai Medical Center,
127 S. San Vicente Blvd, Suite A8113
Los Angeles CA, 90048
Email: jmanuel.perez@cshs.org

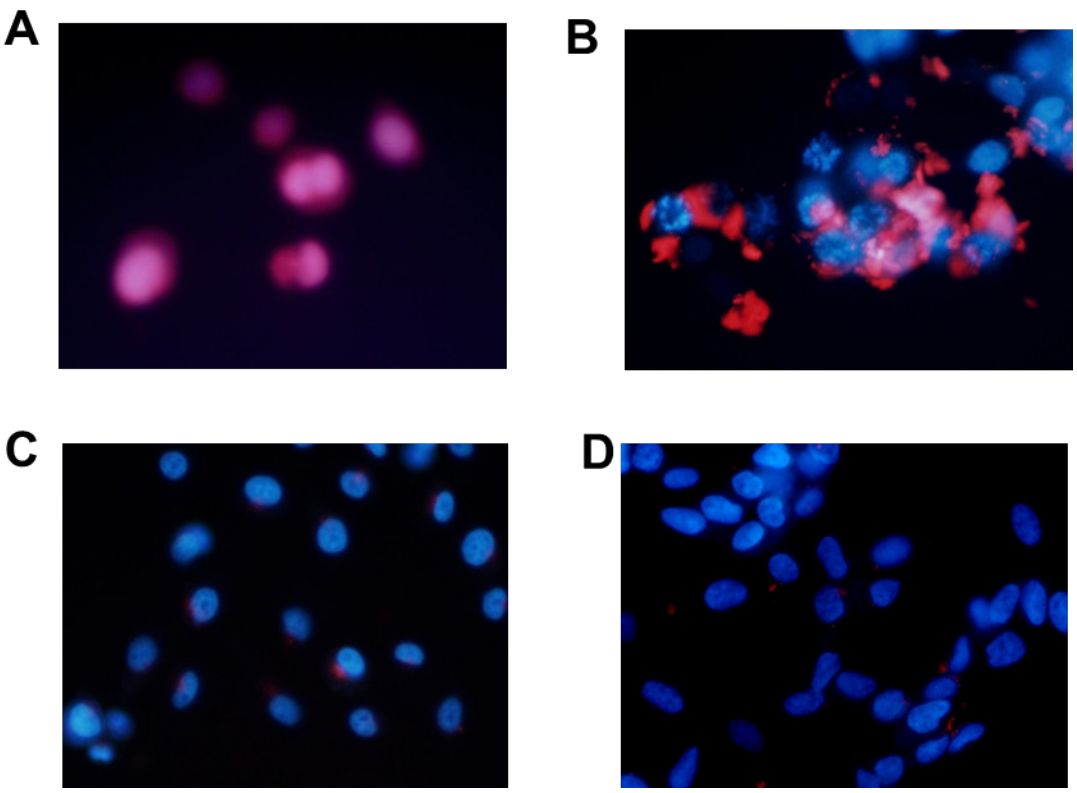

Figure S1. Fluorescence microscopy images of PSMA(+) PC3 (**A**) and LNCaP (**B**) cell lines incubated with Folate-s-s-Doxo probe for 24 hours. Control experiments were done by pre-incubating the PSMA(+) PC3 (**C**) and LNCaP (**D**) cell lines with 2-PMPA before incubation with Folate-s-s-Doxo probe for 24 hours.

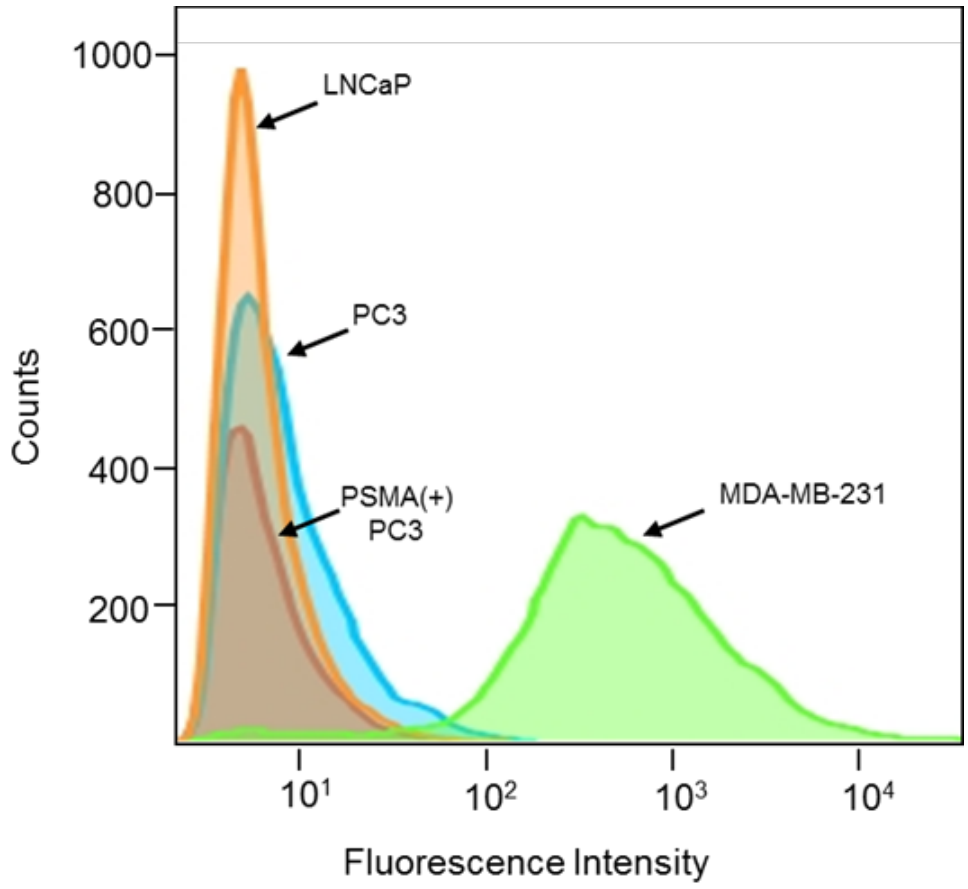

Figure S2. Folate receptor cell surface expression studies by flow cytometry of prostate cancer cells (LNCaP, PC3 and PSMA(+) PC3). The breast cancer cell line MDA-MB-231 was used as a positive control

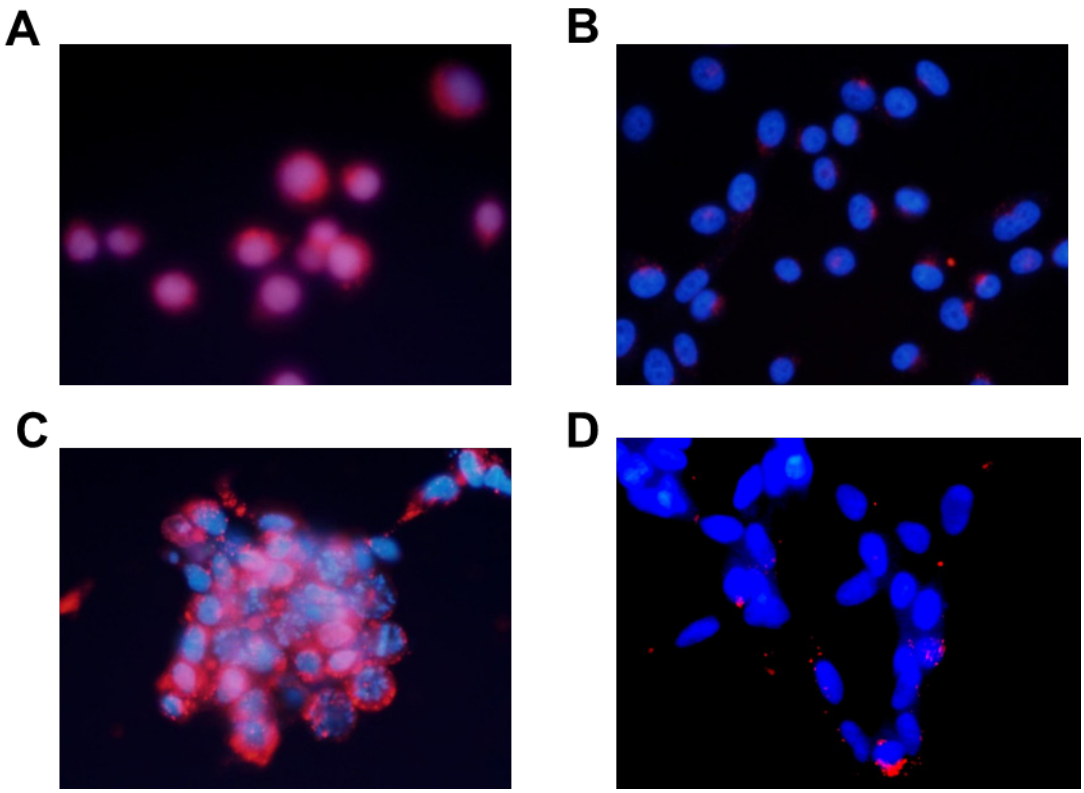

Figure S3. Fluorescence microscopy images of PSMA(+) PC3 cell incubated with Folate-HBPE(CT20p) for 24 hours (**A**), and pre-incubated with PMPA before treatment (**B**). Fluorescence microscopy images of LNCap cell incubated with Folate-HBPE(CT20p) for 24 hours (**C**), and pre-incubated with PMPA (**D**). Nuclei is labeled with DAPI (blue), DiI is red. Cell death is observed after 24 hours of incubation with Folate-HBPE(CT20p) only in PSMA expressing cells (**A** and **C**). This effect is abrogated when the cells are pre-incubated with 2-PMPA, a selective PSMA inhibitor (B and D).

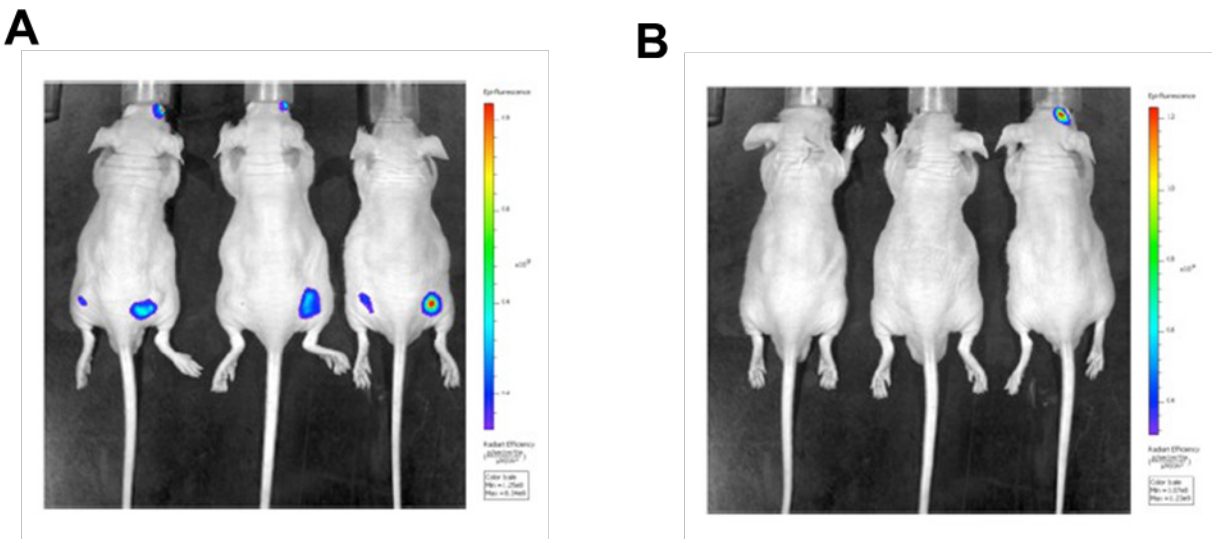

Figure S4. Fluorescence in vivo imaging of mice injected with Folate-HBPE(DiR) (**A**) and HBPE(DiR) without conjugated Folate as control (**B**).

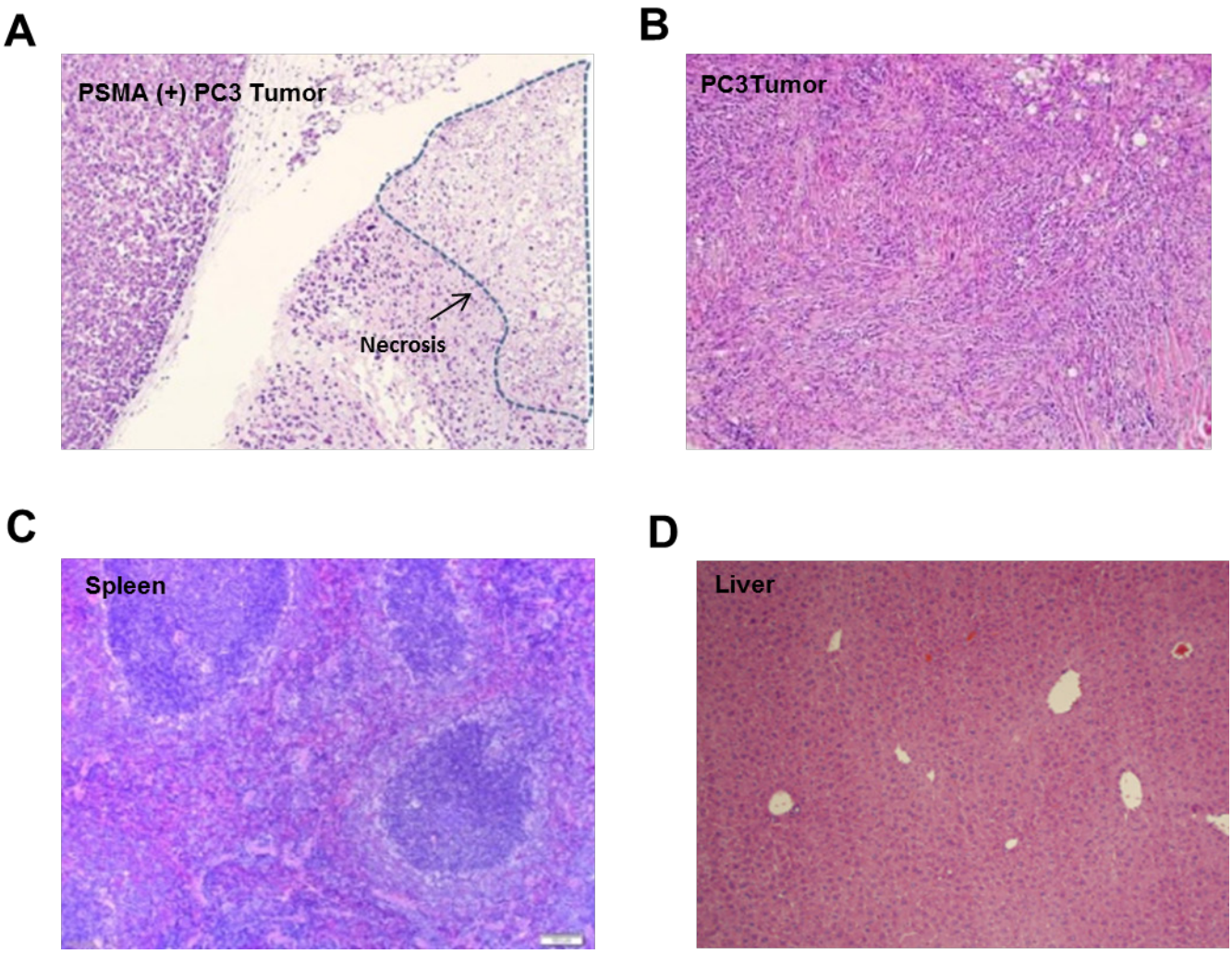

Figure S5. Histological examination of mouse tissues after one-week treatment with Folate HBPE(CT20)p. Necrotic and fragmented tissue is observed in the PSMA(+) tumor (**A**), while no damage is observed in the while type (PSMA(-)) PC3 tumor (**B**). No visible tissue damage was observed in the spleen (C) or liver (D) tissue. 40X magnification in all images

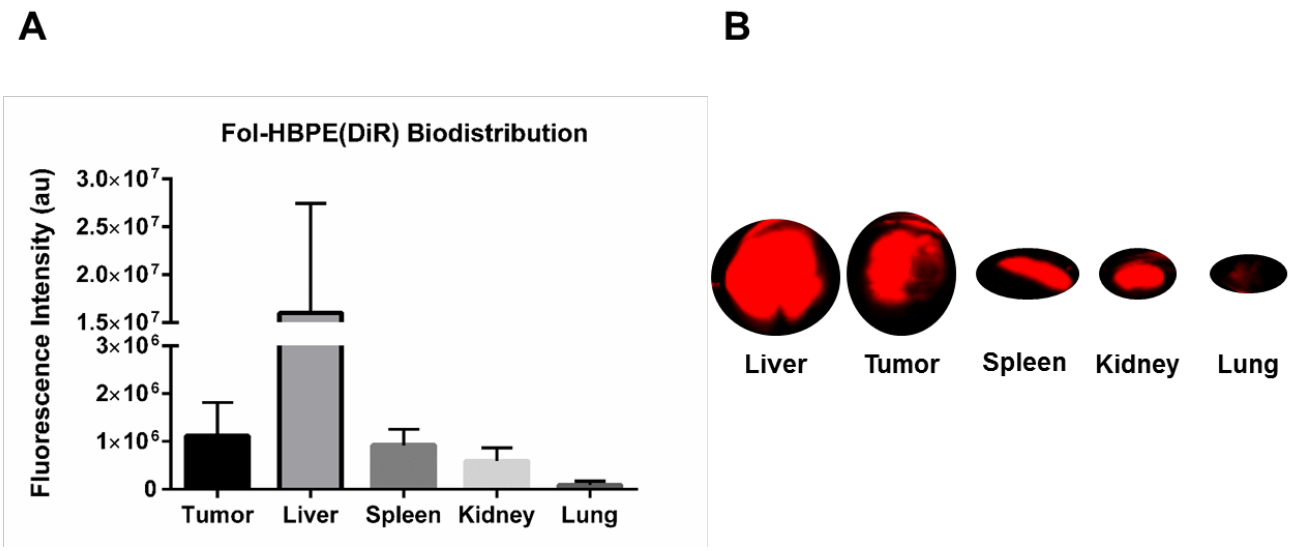

Figure S6. Biodistribution of Folate-HBPE(DiR) nanoparticles in LNCaP bearing mice. Fluorescence intensity of different organs (**A**). Accumulation is seen in the LNCaP tumor, with a large accumulation in liver and spleen as expected for polymeric nanoparticles. Fluorescence images of different organs and the LNCaP tumors (**B**). Image and fluorescence intensity values were obtained in a LI-COR Odyssey Imaging System.

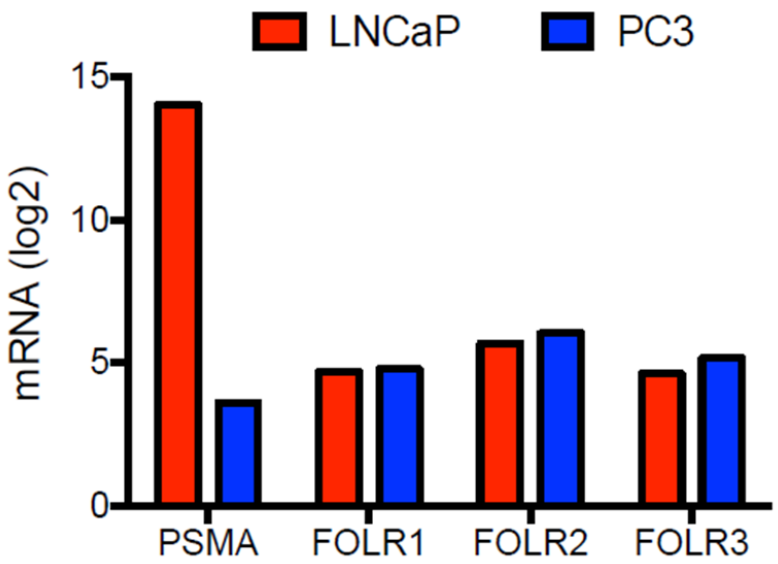

Figure S7. mRNA levels of PSMA and Folate Receptors (FR) 1, 2 or 3 in LNCaP and PC3. Data obtained using a public gene expression database (CAportal)