

BIOGRAPHICAL SKETCH

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NAME: Anthony Frank Shields

eRA COMMONS USER NAME (credential, e.g., agency login): ashields

POSITION TITLE: Professor of Oncology and Medicine

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	BS	06/1974	Biology
Massachusetts Institute of Technology, Cambridge, MA	BS	06/1974	Chemistry
Harvard Medical School, Boston, MA	MD	06/1979	Medicine
Massachusetts Institute of Technology, Cambridge, MA	PhD	06/1979	Cell Biology
University of Washington, Seattle, WA		06/1981	Internal Medicine Residency
University of Washington, Seattle, WA		06/1984	Oncology Fellowship

A. Personal Statement

I am the Associate Center Director for Clinical Sciences under the auspices of the Cancer Center Core Grant at Wayne State University/ Karmanos Cancer Institute (WSU/KCI). My training as a medical oncologist and background in PET imaging accounts for my professional and personal suitability to provide perspectives in oncology, imaging research and teaching graduate and medical students. My translational role in research began as a graduate student when I first mapped the abl-oncogene and studied its role in leukemia in mice. In the clinic, my work concentrates on the treatment of patients with gastrointestinal (GI) cancers with an emphasis on colorectal and pancreatic cancers. I have led and participated in numerous clinical trials for these cancers ranging from phase I to III. This includes serving as co-leader of the stage III adjuvant colon cancer study in the US with almost 2500 patients. My laboratory developed ^{18}F -FLT PET (3'-deoxy-3'-fluorothymidine) and it has been used in national studies (ACRIN 6688) to monitor patients with breast cancer. My insight guides others in the appropriate use of imaging studies in patients with cancer and my foresight helps others design sound imaging studies in cells, animals and humans. I have a broad understanding in clinical sciences with experience that spans from protocol design and development to implementation from the local to the national level. I have been active in cooperative groups such as ECOG-ACRIN and SWOG and I serve on the NCI Colon Task Force, which is charged with overseeing clinical trials for colorectal cancer. At ECOG-ACRIN, I am co-chair of the biomarker committee and I work to integrate new imaging approaches into early trials. I was also a leader of the National Oncology PET Registry (NOPR) where the use of ^{18}F -FDG and Na^{18}F PET was studied in over 400,000 patients. I have taught writing clinical trials as a faculty member in the RSNA weeklong course for over ten years. As a member of the WSU Phase I IRB I help in the evaluation and oversight of new therapeutic agents. With over 30 years of imaging research and clinical experience with drug discovery and development I have been the PI or co-investigator on over 500 clinical trials. I provide clinical perspectives and education on the use of new agents for patients with cancer. These experiences are consistent for my role as Associate Center Director for Clinical Sciences as described in this proposal.

1. Shields A, Goff S, Paskind M, Otto G, and Baltimore D. Structure of the Abelson murine leukemia virus genome. *Cell*, 18:955-962, 1979. PMID: 229975.
2. Shields AF, Grierson JR, Dohmen BM, Machulla H-J, Stayanoff JC, Lawhorn-Crews JM, Obradovich JE, Muzik O, Mangner TM. Imaging proliferation in vivo with [F-18]FLT and positron emission tomography. *Nature Medicine*, 4: 1134-1136, 1998. PMID: 9809561.
3. Grothey A, Sobrero AF, Shields AF, Yoshino T, Paul J, Taieb J, Souglakos J, Shi Q, Kerr R, Labianca R, Meyerhardt JA, Vernerey D, Yamanaka T, Boukovinas I, Meyers JP, Renfro LA, Niedzwiecki D, Watanabe T, Torri V, Saunders M, Sargent DJ, Andre T, Iveson T. Duration of adjuvant chemotherapy for stage III colon cancer. *N Engl J Med*. 378:1177-1188. 2018. PMID: 29590544 .
4. Philip PA, Zaluskpi MM, Vaitkevicius VK, Arlauskas PL, Chaplen R, Heilbrun LK, Weaver D, Shields AF. Phase II study of gemcitabine and cisplatin in the treatment of patients with advanced pancreatic carcinoma. *Cancer*, 92:569-77, 2001. PMID: 11505401.

B. Positions and Honors

Positions and Employment

1985 -1995	Assistant Member, Division of Clinical Research, Hutchinson Cancer Research Ctr, Seattle, WA
1987 -1993	Assistant Professor of Medicine, Division of Oncology, U of WA School of Medicine, Seattle, WA
1987 -1995	Staff Physician, VA Medical Center, Seattle, Washington
1993 -1995	Associate Professor of Medicine, Div of Oncology, U of WA School of Medicine, Seattle, WA
1995 -1999	Associate Professor of Medicine and Oncology, (tenured) Wayne State University School of Medicine, Detroit, Michigan
1995 -2006	Chief, GI Oncology Section, Karmanos Cancer Institute, Harper University Hospital and the Detroit Medical Center
1997 -2012	Program Leader, Developmental Therapeutics, Karmanos Cancer Institute
2012 -2015	Program Leader, Molecular Imaging Program, Karmanos Cancer Institute
2015 -2018	Intergovernmental Personnel, National Cancer Institute, Cancer Imaging Program, Washington, DC
1999 -	Professor, Oncology and Medicine, (tenured) Wayne State Univ School of Medicine, Detroit, MI
2003 -	Associate Center Director for Clinical Sciences, Karmanos Cancer Institute, Detroit, MI
2005 -	Faculty Member, Cancer Biology Graduate Program, Wayne State School of Medicine

Board Certification and Licensing

Board certified in Internal Medicine # 85200
 Board certified in Hematology # 85200
 Board certified in Medical Oncology # 85200
 Medical License, State of Michigan #4301065008

Other Experience and Professional Memberships

1995 -	Scientific Member, Karmanos Cancer Institute
2000, 2004-05	Chair, Michigan Department of Community Health Task Force on Colorectal Cancer
2014 -	Disease Group Lead, GI Oncology, Caris Life Sciences
2017 -	ECOG-ACRIN Principal Investigator, Scientific Planning, and Nomination Committees

Honors

1983 -1985	National Research Service Award Fellow
1984 -1985	American Cancer Society Junior Faculty Fellow
1999 -2004	Midcareer Investigator Award, National Cancer Institute
2005	Peter Valk Distinguished Clinical Scientist Award, Academy of Molecular Imaging
2007	Wayne State University Distinguished Faculty Fellowship Award

C. Contributions to Science

1. As a fellow, I began work on the development and testing labeled thymidine of tracers for use with PET. My early career goal of imaging proliferation led to the development of ^{18}F -FLT(3'-deoxy-3'-fluorothymidine) for PET and it is now available under an IND from the FDA and is being tested in centers worldwide. I lead national and local efforts to analyze the kinetics of ^{18}F -FLT retention from data obtained as part of clinical studies.
 - a. Shields AF, Larson SM, Grunbaum Z, and Graham MM. Short- term thymidine uptake in normal and neoplastic tissues: Studies for PET. *J Nucl Med*, 25:759-764, 1984. PMID: 6610731.
 - b. Shields AF, Lawhorn-Crews JM, Briston DA, Zalzala S, Gadgeel S, Douglas KA, Mangner TJ, Heilbrun LK, Muzik O. Analysis and reproducibility of [^{18}F] 3'-deoxy-3'-fluorothymidine PET imaging in patients with non-small cell lung cancer. *Clin. Cancer Res*, 14:4463-8, 2008. PMID: 1862846.
 - c. Kostakoglu L, Duan F, Idowu MO, Jolles PR, Bear HD, Muzi M, Cormack J, Muzi JP, Pryma DA, Specht HM, Hovanessian-Larsen L, Miliziano J, Mallett S, Shields AF, Mankoff DA. A Phase II study of [^{18}F]-3'-deoxy-3'-fluorothymidine positron emission tomography (FLT-PET) in the assessment of early response of breast cancer to neoadjuvant chemotherapy: results from ACRIN 6688. *J Nucl Med*. 56:1681-9. 2015. PMID 26359256.
 - d. McHugh CI, Thipparthi MR, Lawhorn-Crews JM, Polin L, Gadgeel S, Akoury J, Mangner TJ, Douglas KA, Li J, Ratnam M, Shields AF. Utilizing Radiolabeled 3'-deoxy-3'-[^{18}F]fluorothymidine with positron emission tomography to monitor the effect of dexamethasone on non-small cell lung cancer. *J Nucl Med*. 59:1544-1550, 2018. PMID: 29674424.
2. My clinical career has also included developing new treatment for patient with pancreatic and colorectal cancer. These span from Phase I to multi-center trials and incorporates PET to monitor clinical outcomes.
 - a. Choi M, Heilbrun LK, Venkatramanamoorthy R, Lawhorn-Crews JM, Zalupski MM, Shields, AF. Using ^{18}F Fluorodeoxyglucose Positron Emission Tomography (FDG PET) to monitor clinical outcomes in patients treated with neoadjuvant chemo-radiotherapy for locally advanced pancreatic cancer. *Am J Clin Oncol*, 33:257-61, 2010. PMID: 19806035.
 - b. Shields AF, Zalupski MM, Marshall JL, Meropol NJ. Treatment of advanced colorectal cancer with oxaliplatin and capecitabine: a phase II trial. *Cancer*, 100:531-7, 2004. PMID: 14745869.
 - c. Alberts SR, Sargent DJ, Nair S, Mahoney MR, Mooney M, Thibodeau SN, Smyrk TC, Sinicrope FA, Chan E, Gill S, Kahlenberg MS, Shields AF, Quesenberry JT, Webb TA, Farr GH Jr, Pockaj BA, Grothey A, Goldberg RM. Effect of oxaliplatin, fluorouracil, and leucovorin with or without cetuximab on survival among patients with resected stage III colon cancer: a randomized trial. *JAMA*. 307:1383-93. 2012. PMID: 22474202.
 - d. Ramanathan RK, McDonough SL, Philip PA, Hingorani SR, Lacy J, Kortmansky JS, Thumar J, Chiorean EG, Shields AF, Behl D, Mehan PT, Gaur R, Seery T, Guthrie KA, Hochster HS. Phase IB/II randomized study of FOLFIRINOX plus pegylated recombinant human hyaluronidase versus FOLFIRINOX alone in patients with metastatic pancreatic adenocarcinoma: SWOG S1313. *J Clin Oncol*, 37:1062-1069. 2019. PMID: 30817250.
3. In addition, I also studied the use of a number of other PET tracers. For example, I helped develop the synthesis of ^{18}F -FMAU {1-(2'-deoxy-2'-fluoro-beta-D-arabinofuranosyl)-thymine}, which was previously only available labeled with ^{11}C . This agent has been used to study patients with prostate cancer. I also work with labeled therapeutic agents, such as, ^{64}Cu -nanoparticles and ^{18}F -FAU to study drug distribution as part of Phase I clinical trials.
 - a. Sun H, Sloan A, Mangner TJ, Vaishampayan U, Muzik O, Collins JM, Douglas K, and Shields AF. Imaging DNA synthesis with ^{18}F -FMAU and positron emission tomography in patients with cancer. *Eur J Nucl Med Mol Imaging*, 32:15-22, 2005. The European Association of Nuclear Medicine and Springer-Verlag Award - Best Clinical Paper, 2005. PMID: 15586282.
 - b. Nimmagadda S, Mangner TJ, Douglas KA, Muzik O, Shields AF. Biodistribution, PET imaging, and radiation dosimetry estimates of HSV-tk gene expression imaging agent (1-(2'-deoxy-2'-[^{18}F]-fluoro- β -D-arabinofuranosyl)-5-iodouracil) in normal dogs. *J Nucl Med*, 48:655-660,

2007. *Society of Nuclear Medicine Education and Research Foundation, Alavi-Mandell Award*, 2008. PMID: 17401105.

- c. Blocker, SJ, Douglas KA, Polin LA, Lee H, Hendricks BS, Lalo E, Chen W, Shields AF. Liposomal ⁶⁴Cu-PET imaging of anti-VEGF drug effects on liposomal delivery to colon cancer xenografts. *Theranostics*. 7:4229-39, 2017. PMID: 2915882.
 - d. Vaishampayan U, Podgorski I, Heilbrun LK, Lawhorn-Crews JM, Dobson KC, Boerner JL, Stark K, Smith D, Heath EI, Fontana J, Shields AF. Biomarkers and bone imaging dynamics associated with clinical outcomes of oral cabozantinib therapy in metastatic castrate resistant prostate cancer. *Clin Cancer Res*. 25:652-662, 2019. PMID: 30327304.
4. I helped lead national trials on the use of PET, including over 400,000 patients studied as part of the National Oncology PET Registry (NOPR).
- a. Hillner BE, Siegel BA, Shields AF, Liu D, Gareen IF, Hanna L, Stine SH, Coleman RE. The impact of Positron Emission Tomography on expected management during cancer treatment: findings of the National Oncologic PET Registry. *Cancer*, 115:410-8, 2009. PMID: 19016303.
 - b. Subramaniam RM, Shields AF, Sachedina A, Hanna L, Duan F, Siegel BA, Hillner BE. Impact on patient management of [18F]-fluorodeoxyglucose Positron Emission Tomography (PET) used for cancer diagnosis: analysis of data from the national oncologic PET registry. *Oncologist*. 21:1079-84, 2016. PMID: 27401896.
 - c. Hillner BE, Siegel BA, Hanna L, Duan F, Quinn B, Shields AF. 18F-Fluoride PET used for treatment monitoring of systemic cancer therapy: results from the National Oncologic PET Registry. *J Nucl Med*. 56:222-8. 2015. PMID 25593113.
 - d. Weber WA, Gatsonis CA, Mozley PD, Hanna LG, Shields AF, Aberle DR, Govindan R, Torigian DA, Karp JS, Yu JQ, Subramaniam RM, Halvorsen RA, Siegel BA. Repeatability of 18F-FDG PET/CT in advanced non-small cell lung cancer: prospective assessment in two multicenter trials. *J Nucl Med*. 56:1137-43. 2015. PMID 25908829.
5. My clinical career has included the study of both imaging and molecular biomarkers to understand cancer and its prognosis and response to therapy.
- a. Lee H, Shields AF, Siegel BA, Miller KD, Krop I, Ma CX, LoRusso PM, Munster PN, Campbell K, Gaddy DF, Leonard SC, Geretti E, Blocker SJ, Kirpotin DB, Moyo V, Wickham TJ, Hendricks BS. ⁶⁴Cu-MM-302 Positron emission tomography quantifies variability of enhanced permeability and retention of nanoparticles in relation to treatment response in patients with metastatic breast cancer. *Clin Cancer Res*. 23:4190-4202, 2017. PMID: 28298546.
 - b. Ang C, Shields A, Xiu J, Gatalica Z, Reddy S, Salem ME, Farhangfar C, Hwang J, Astsaturon I, Marshall JL. Molecular characteristics of hepatocellular carcinomas from different age groups. *Oncotarget*. 8:101591-101598. 2017. PMID: 29254188.
 - c. Salem ME, Weinberg BA, Xiu J, El-Deiry WS, Hwang JJ, Gatalica Z, Philip PA, Shields AF, Lenz, H-J, Marshall JL. Comparative molecular analyses of left-sided colon, right-sided colon, and rectal cancers. *Oncotarget*. 8:86356-68. 2017. PMID: 29156800.
 - d. Tokunaga R, Xiu J, Johnston C, Goldberg RM, Philip PA, Seeber A, Naseem M, Lo JH, Arai H, Battaglin F, Puccini A, Berger MD, Soni S, Zhang W, Hwang JJ, Shields AF, Marshall JL, Baba H, Korn WM, Lenz HJ. Molecular profiling of appendiceal adenocarcinoma and comparison with right-sided and left-sided colorectal cancer. *Clin Cancer Res*. 25:3096-3103. 2019. PMID: 30692096.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NCI UG1CA233163 L Flaherty and A Shields (PIs) 3/5/2019-2/28/2025

NCI National Clinical Trials Network – Network Lead Academic Participating Site

The relationship between WSU/KCI and the NCTN has been built on the foundational premise that multidisciplinary clinical research provides the best treatment option for patients with cancer. Our goal over the next few years is to extend that level of commitment and participation through the McLaren community cancer research network within the State of Michigan.

NCI 5P30-CA22453-23 Bepler, Gerold (PI) 12/01/20 -11/30/25

Cancer Center Support Grant

Dr. Shields serves as Associate Center Director for Clinical Sciences and co-leader of the Molecular Imaging Program. The major goals are for research infrastructure of the comprehensive cancer center grant. Roles: Senior Leadership and past Program Leader

NCI U01 CA199240 AG Schwartz and T Albrecht (PIs) 2/27/2017 -1/31/2022

Detroit Research on Cancer Survivors (Detroit ROCS)

The overall goal is to better understand major factors affecting cancer progression, recurrence, mortality and quality of life in Africa American cancer survivors. Role: Co-Investigator

Completed Research Support

W81XWH-15-1-0171 Shields, Anthony (contact PI) 09/30/15 -09/29/19

Department of Defense: Lung Cancer Research Program, Clinical Exploration Award (*Clinical Trials Category*)
Exploring mechanisms and predictors of treatment response to improve outcome of standard chemotherapy in non-small cell lung cancer

The overall goals are to study FLT-PET as a functional approach to assess the effect of Dexamethasone (Dex) on treatment for non-small cell lung cancer and to validate tumor GR status as a biomarker of tumor Dex sensitivity and to compare GR status and levels of biomarkers to FLT retention. (Ratnam, Manohar and Matherly Lawrence, Co-PIs)

U01CA153606 Albrecht, Terrance (PI) 9/1/14 -8/31/17

Southeast Michigan Community Network Program

The major goal of this study is to continue our vibrant, comprehensive, and sustainable program to reduce disparities in breast, prostate, lung, and colorectal cancers that adversely affect older, underserved, African American adults in southeast Michigan. Role: Co-investigator

R01 CA182526 Lum, Lawrence (PI) 7/1/14-8/31/16

NIH/NCI: Targeting Neuroblastoma with Armed T cells

The overall goal is to conduct a phase I/II dose escalation trial in high risk patients with neuroblastoma and other GD2+ pediatric tumors using activated T cells armed with anti-CD3 x humanized anti-GD2 bispecific antibody to determine safety and to determine whether infusions can improve clinical outcomes and induce both adaptive and innate immune responses in patients with high risk neuroblastoma. Role: Co-Investigator

NCI: CA180820-01 Comis, Robert L and Schnall, Mitchell D (Co-PIs) 4/29/14 -2/28/19

NCI: ECOG-ACRIN Network Group Operations Center (U10) RFA-CA-12-010

The overall goal is to incorporate imaging biomarkers into therapeutic trials. Role: Co-Investigator