BIOGRAPHICAL SKETCH

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NAME: **Katherine W. Ferrara**

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POSITION TITLE: Professor of Radiology at Stanford

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pittsburgh, Pittsburgh, PA	B.S.	1976	Biology/Physical Therapy
University of California, Davis, Davis, CA	Ph.D.	1989	Electrical Engineering

A. Personal Statement

My focus is image-guided drug and gene delivery and I am engaged in the design of imaging devices, molecularly-targeted imaging probes and engineered delivery vehicles, drawing upon my education in biology and imaging physics and more than 20 years of experience with the synthesis and labeling of therapeutic particles. My laboratory has unique resources for and substantial experience in synthetic chemistry and ultrasound, CT, MR and PET imaging. My initial academic training was in biology. I followed this with training as a physical therapist, 4 years of clinical experience and a second BS, MS and PhD in engineering. I was a principal project engineer for General Electric Medical Systems from 1983-8 and contributed to the design and development of the early magnetic resonance and ultrasound prototype systems. Following an appointment as an Associate Professor in the Department of Biomedical Engineering at the University of Virginia, Charlottesville, I served as the founding chair of the Department of Biomedical Engineering at UC Davis, now a department of 32 faculty members. Over a period of six years, I developed the departmental educational programs, hired 13 faculty members and funded and developed the facilities before stepping down to focus on my research program. I have been a Distinguished Professor of Biomedical Engineering at UC Davis until my recent move to Stanford. I am a member of the National Academy of Engineering and a fellow of five societies spanning physics, biomedical and electrical engineering. My publications are indexed by ferrara k* and include more than 280 technical manuscripts. Our major contributions include papers in image-guided drug and gene delivery, techniques for radiolabeling nanoparticles, immunotherapeutics, combining focal and immunotherapies, nanoparticle design (including novel temperature sensitive particles and miRNA carriers), and imaging system and transducer design (spanning ultrasound and MRI). Recent papers focus on transfection and enhanced immune system response.

1. Ilovitsh I, Feng Y, Foiret J, Kheirolomoom A, Zhang H, Ingham ES, Ilovitsh A, Tumbale SK, Fite BZ, Wu B, Raie, M, Zhang N, Kare AJ, Chavez M, Qi S, Pelled G, Gazit D, Vermesh O, Steinberg I, Gambhir SS, **Ferrara KW**, Low frequency ultrasound-mediated cytokine transfection enhances T cell recruitment at local and distant tumor sites, Proceedings of the National Academy of Sciences, www.pnas.org/cgi/doi/10.1073/pnas.1914906117, epub May 19, 2020, PMC in process.
2. Seo JW, Ingham ES, Mahakian L, Tumbale S, Wu B, Aghevlian S, Shams S, Baikoghli M, Jain P, Ding X, Goeden N, Dobreva T, Flytzanis NC, Chavez M, Singhal K, Leib R, James ML, Segal DJ, Cheng RH, Silva EA, Gradinaru V, **Ferrara KW**. Positron emission tomography imaging of novel AAV capsids maps rapid brain accumulation, Nature Communications, 2020 Apr 30;11(1):2102. doi: 10.1038/s41467-020-15818-4, PMC in process..
3. Son, D., Kumar S , Takabe W, Kim C , Ni CW , Alberts-Grill N, Jang I, Kim So , Kim WK, Kang SW, Baker AH, Seo JW, **Ferrara KW,** Jo H. (2013) Inhibition of mechanosensitive microRNA, miR-712, atypical microRNA derived from pre-ribosomal RNA, decreases endothelial inflammation and atherosclerosis. Nature Communications, 2013;4:3000. doi: 10.1038/ncomms4000. PMC3923891.

4. Bez M, Sheyn D, Tawackoli W, Avalos P, Shapiro G, Giaconi JC, Da X, David SB, Gavrity J, Awad HA, Bae HW, Ley EJ, Kremen TJ, Gazit Z, **Ferrara KW**, Pelled G, Gazit D. In situ bone tissue engineering via ultrasound-mediated gene delivery to endogenous progenitor cells in mini-pigs. Sci Transl Med. 2017 May 17;9(390). pii: eaal3128. doi: 10.1126/scitranslmed.aal3128, PMC5524999.

B. Positions and Honors

Positions and Employment

1983-1988 Project/System Engineer, General Electric Medical Systems, Ultrasound Division, Rancho Cordova, CA
1989-1995 Associate Professor, California State University, Sacramento
1993-1995 Principal Research Scientist, Riverside Research Institute, New York, NY
1993-2001 Adjunct Associate Professor, Cornell Medical School, New York, NY
1995-1999 Associate Professor, Biomedical Engineering, University of Virginia
1999-2003 Visiting Associate Professor, Biomedical Engineering, University of Virginia
1999-2013 Professor and Chair (Chair through 1/2005), Biomedical Engineering, UC Davis
2013-2018 Distinguished Professor, Biomedical Engineering, UC Davis
2018- Professor of Radiology, Stanford University

Selected Experience and Professional Memberships

2000-2004 Member, NIH Diagnostic Radiology Study Section
2006-2010 Member, NIH NIBIB Advisory Council
2014-2016 Chair, NIH CMIP study section
2019-2021 Member, Board of Scientific Counselors, NIBIB

Selected Honors

Elected Fellow: American Association for the Advancement of Science, IEEE, Acoustical Society of America, Biomedical Engineering Society, American Institute of Medical and Biological Engineers
1995 Terrence Matzuk award from American Institute of Ultrasound in Medicine
1996 Outstanding paper award – IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control
Other outstanding paper awards to laboratory or PI in 1999 (3), 2001, 2003, 2007, 2013
1999 George Thorn award for Biomedical Engineering research, Whitaker Foundation
2006 Mid-career research award – UC Davis College of Engineering.
2012 Senior research award – UC Davis College of Engineering.
2012 IEEE Achievement Award (top award from IEEE ultrasonic society)
2013 Distinguished Professor, Biomedical Engineering, UC Davis
2014 Election to National Academy of Engineering
2017 IEEE Distinguished Lecturer in Ultrasonics
2019 World Molecular Imaging Society Gold Medal, Academy of Radiology Distinguished Investigator, Judith Poole Award from Association of Women in Science
2020 2021 IEEE Biomedical Engineering Award

C. Contributions to Science (h index currently 70)

Enhanced immunotherapeutics

Our laboratory is broadly developing strategies for combined focal and immunotherapies, immune cell imaging and nanovaccines.

5. Chavez M, Silvestrini MT, Ingham ES, Fite BZ, Mahakian LM, Tam SM, Ilovitsh A, Monjazeb AM, Murphy WJ, Hubbard NE, Davis RR, Tepper CG, Borowsky AD, **Ferrara KW**, Distinct immune signatures in directly treated and distant tumors result from TLR adjuvants and focal ablation. Theranostics 2018; 8(13): 3611-3628. doi:10.7150/thno.25613.
6. Kakwere H, Ingham ES, Allen R, Mahakian LM, Tam SM, Zhang H, Silvestrini MT, Lewis JS and **Ferrara KW**, Towards personalized peptide-based cancer nanovaccines: a facile and versatile synthetic approach, Bioconjugate Chemistry, 2017 Nov 15;28(11):2756-2771. doi: 10.1021/acs.bioconjchem.7b00502. Epub 2017 Oct 13. PMC5687982.
7. Kakwere H, Ingham ES, Allen R, Mahakian LM, Tam SM, Zhang H, Silvestrini MT, Lewis JS and **Ferrara KW**, Unimicellar hyperstars as multi-antigen cancer nanovaccines displaying clustered epitopes of immunostimulating peptides, RSC Biomaterials Science, in press.
8. Silvestrini MT, Ingham ES, Liu Y, Fite BZ, Mahakian LM, Tam SM, Kheirolomoom A, Tucci S, Watson KD, Wong A, Monjazeb A, Hubbard NE, Murphy WJ, Borowsky AD, **Ferrara KW**, Incorporation of image-guided thermal ablation into immunotherapy protocols: priming is key to effective therapy, Journal of Clinical

Investigation Insight, 2017 Mar 23;2(6):e90521. doi: 10.1172/jci.insight.90521, PMC5358490.

Image-guided drug/gene delivery

In the area of image-guided drug and gene delivery, my laboratory has created and applied some of the first PET labeling strategies and quantitative methods for tracking nanotherapeutic pharmacokinetics and efficacy and have published approximately 20 papers in this area. These probes and strategies have subsequently been used by multiple investigators tracking iron oxide particles, solid lipid nanoparticles, triple helix micelles and other novel nanotherapeutics. In Watson et al, we demonstrate the use of hyperthermia to enhance the delivery of long circulating particles. In Rygh et al and Hamzah et al, we applied our unique strategies to track

9. Seo JW, Mahakian LM, Silvestrini MT, Tam S, Ingham ES, Salazar FB, Borowsky AD, Wu AM, and **Ferrara KW**, CD8 T-cell density imaging with 64Cu-labeled cys-diabody informs immunotherapy-related protocols, Clin Cancer Res. 2018 Jul 2. pii: clincanres.0261.2018. doi: 10.1158/1078-0432.CCR-18-0261.
10. Kheirolomoom A, Kim CW, Seo JW, Kumar S, Son DJ, Gagnon MK, Ingham ES, **Ferrara, KW#**, Jo H#, Site-specific delivery of anti-miR-712 by VCAM1-targeting liposomal nanoparticles prevents atherosclerosis in ApoE-knockout mice, ACS Nano, # indicates co-senior authors, ACS Nano. 2015 Sep 22;9(9):8885-97. doi: 10.1021/acsnano.5b02611. PMC4581466.
11. Thorsen F, Fite B, Mahakian LM, Seo JW, Qin S, Harrison V, Johnson S, Ingham E, Caskey C, Sundstrøm T, Meade TJ, Harter PN, Skaftnesmo KO, **Ferrara KW**. Multimodal imaging enables early detection and characterization of changes in tumor permeability of brain metastases. J Control Release. 2013 Dec 28;172(3):812-22. PMC3922207. (2013 outstanding paper award)
12. Watson KD, Lai CY, Qin S, Kruse DE, Lin YC, Seo JW, Cardiff RD, Mahakian LM, Beegle J, Ingham ES, Curry FR, Reed RK, **Ferrara KW**. Ultrasound increases nanoparticle delivery by reducing intratumoral pressure and increasing transport in epithelial and epithelial-mesenchymal transition tumors, Cancer Research, 2012 Mar 15;72(6):1485-93. Epub 2012 Jan 26. PMC3357123.

Nanoparticle design and characterization

My laboratory has created several unique nanoparticles that are now advancing toward translation. We demonstrated the ability to create a far more stable doxorubicin liposome by creating a fine crystal between doxorubicin and copper. We have also developed molecularly-targeted vehicles for cardiovascular disease. For example, in Zhang et al we show that targeted nanoparticles accumulate to 40% injected dose/cc on the heart endothelium within 1 minute and remain bound for hours. In subsequent papers, we demonstrated the ability to track the cargo across the endothelium using optical imaging and have a paper under review regarding successful targeted miRNA delivery vehicles. In Dong et al and subsequent papers, we collaborate with the Xu laboratory with a goal of developing a 15 nm vehicle for the delivery of peptide and small molecule therapeutics that have substantial advantages in glioblastoma.

13. Kheirolomoom A, Ingham ES, Mahakian LM, Tam SM, Silvestrini MT, Tumbale SK, Foiret JL, Hubbard NE, Borowsky AD, Murphy WJ, **Ferrara KW**, CpG Expedites Regression of Local and Systemic Tumors when Combined with Activatable Nanodelivery, J Control Release. 2015 Dec 28;220(Pt A):253-64. doi: 10.1016/j.jconrel.2015.10.016. PMC4688109.
14. Zhang H, Kusunose J, Kheirolomoom A, Seo JW, Qi J, Watson KD, Lindfors HA, Ruoslahti E, Sutcliffe JL, **Ferrara KW**. Dynamic imaging of arginine-rich heart-targeted vehicles in a mouse model. Biomaterials. 2008; 29:1976-88. PMC2475513.
15. Dong H, Dube N, Shu JY, Seo JW, Mahakian LM, **Ferrara KW**, Xu T. Long Circulating Micelles Stabilized By Directional Repulsive Forces. ACS Nano. 2012 Jun 26; 6(6):5320-9. PMC3531550.
16. Kheirolomoom A, Lai CY, Tam SM, Mahakian LM, Ingham ES, Watson KD, **Ferrara KW**. Complete regression of local cancer using temperature-sensitive liposomes combined with ultrasound-mediated hyperthermia. J Control Release. 2013 Nov 28;172(1):266-73. PMC3037269.

Novel therapies

My laboratory has also collaborated with groups developing new therapeutics. We have conducted the *in vivo* research studies and have developed imaging methods to assess therapeutic response. In Zhang et al, we examined the effect of omega 3 fatty acids and soluble epoxide hydrolase inhibition on cancer, demonstrating a reduction in tumor growth. In Wong et al and Bez et al, we developed new methods for enhanced drug and gene delivery.

17. Zhang G, Panigrahy D, Mahakian LM, Yang J, Liu JY, Stephen Lee KS, Wettersten HI, Ulu A, Hu X, Tam S, Hwang SH, Ingham ES, Kieran MW, Weiss RH, **Ferrara KW**, Hammock BD. Epoxy metabolites of

docosahexaenoic acid (DHA) inhibit angiogenesis, tumor growth, and metastasis. Proc Natl Acad Sci U S A. Proc Natl Acad Sci U S A. 2013 Apr 16;110(16):6530-5. PMC3631682.
18. Zhang G, Panigrahy D, Hwang SH, Yang J, Mahakian LM, Wettersten HI, Liu JY, Wang Y, Ingham ES, Tam S, Kieran MW, Weiss RH, **Ferrara KW**, Hammock BD. Dual inhibition of cyclooxygenase-2 and soluble epoxide hydrolase synergistically suppresses primary tumor growth and metastasis. Proc Natl Acad Sci U S A. 2014 Jul 29;111(30):11127-32. PMC4121808.
19. Wong AW, Fite BZ, Liu Y, Kheirolomoom A, Seo JW, Watson KD, Mahakian LM, Tam SM, Zhang H, Foiret J, Borowsky AD, **Ferrara KW.** Ultrasound ablation enhances drug accumulation and survival in mammary carcinoma models. J Clin Invest. 2015 Nov 23. pii: 83312. doi: 10.1172/JCI83312. PMC4701551.
20. Bez M, Kremen TJ, Tawackoli W, Sheyn D, Shapiro G, Giaconi JC, **Ferrara KW**, Gazit D, Pelled G, Ultrasound-mediated Gene Delivery Enhances Tendon Allograft Integration in Mini-pig Ligament Reconstruction, Mol Ther. 2018 Apr 26. pii: S1525-0016(18)30193-X.

Imaging design

My laboratory has also had a significant component of system design including advanced methods to bring optical techniques to ultrasound, MRI thermometry at high field (7T).

21. Ilovitsh T, Ilovitsh A, Foiret J, Fite BZ, and **Ferrara KW**, Acoustical structured illumination for super-resolution ultrasound imaging, Communications Biology, (a new Nature Journal), volume 1, Article number: 3 (2018) doi:10.1038/s42003-017-0003-5, PMC5988254.
22. Ilovitsh T, Ilovitsh I, Foiret J, and **Ferrara KW**, Imaging beyond ultrasonically-impenetrable objects, Scientific Reports, Sci Rep. 2018 Apr 10;8(1):5759. doi: 10.1038/s41598-018-23776-7, PMC5893560.
23. Fite BZ, Liu Y, Kruse DE, Caskey CF, Walton JH, Lai CY, Mahakian LM, Larrat B, Dumont E, **Ferrara KW**, Magnetic Resonance Imaging at 7T for Real-Time Monitoring and Correction of Ultrasound Induced Mild Hyperthermia, PLoS One, 2012;7(4):e35509. Epub 2012 Apr 20. PMC3335017.
24. Liu Y, Fite BZ, Mahakian LM, Johnson SM, Larrat B, Dumont E, **Ferrara KW**. Concurrent Visualization of Acoustic Radiation Force Displacement and Shear Wave Propagation with 7T MRI. PLoS One. 2015 Oct 6;10(10):e0139667. doi: 10.1371/journal.pone.0139667. PMC4594908.

List of My Refereed Journal Papers in PubMed

http://www.ncbi.nlm.nih.gov/pubmed/?term=ferrara+katherine+OR+ferrara+kw+OR+(Ferrara+k+and+(morgan+k+or+dayton+p))

I also have a Google Scholar page that is complete and can be accessed from:
http://scholar.google.com/citations?user=7mTBiAQAAAAJ&hl=en

D. Research Support

Ongoing Research Support

1R01CA211602 (MPI: Ferrara) 03/08/17 – 02/28/22
NIH/NCI
Large aperture and wideband modular ultrasound arrays for the diagnosis of liver cancer
We are developing large transducer arrays.

R01CA210553 (PI: Ferrara) 07/01/16 – 06/30/21
NIH/NCI
Image-guided ultrasound therapy and drug delivery in pancreatic cancer
We are developing a temperature-sensitive gemcitabine liposome and squalene-gemcitabine particles and applying them with hyperthermia.

R01CA199658 (PI: Ferrara) 07/01/15 – 010/31/20
NIH/NCI
Optimized ultrasound-enhanced immunotherapy
Project involves the development of ultrasound-guided drug delivery with hyperthermia and ultrasound thermometry.

R01CA112356 (PI: Ferrara) 07/01/05 – 06/30/23
NIH/NCI
Insonation of ultrasound microbubbles at low frequency to enhance image-guided therapy
The objective of this project is to create sensitive and specific ultrasound strategies capable of detecting small tumors using ultrasound and targeted microbubbles.

1R01EB028646-01 (PI: Ferrara) 08/01/18 – 03/31/22
NIH/NIBIB
In vivo PET imaging of novel engineered AAVs informs capsid design
The goal of this project is to use PET to optimize AAV capsids.

R01CA227687-01 (PI: Butts-Pauly) 03/01/18 – 02/28/23
NIH/NCI
The Impact of FUS-Mediated Brain Cancer Therapy on BBB Transport, Cytokines, and Immunocyte Trafficking
The goal is to assess the safety and efficacy of BBB transport as a function of ultrasound parameters.
Role on Project: *Co-investigator*

R01EB026094 (PI: Gazit) 04/01/18 – 03/31/23
NIH/NIBIB
Ultrasound-guided DNA delivery for regenerative medicine
The goal is to transfect stem cells to enhance healing of bone and ligaments.
Role on Project: *Co-investigator*

FUSF/Parker Institute Cancer Immunotherapy/CRI (PI: Ghanouni) (Start date is pending)
Trial of MRgFUS ablation in pancreatic cancer
Goal is to treat 10 patients with ablation and standard of care chemotherapy to gain safety data
Role on Project: Co-investigator

Focused Ultrasound Surgery Foundation (PI: Ferrara) 01/01/2020 - 12/31/2020
αCD40 + Ablation trial
Major goal: Characterize the response to aCD40 and ablation in pancreatic cancer.

Stanford Tübingen Grant (PI: Ferrara) 01/01/2020 - 12/31/2020
Applying aCD40 as a new imaging biomarker for immune cells (based on RNAseq)
Major Goal: Create a collaboration with Tübingen for immunoPET.

Completed Research Support (past 3 years)

6143-1089-03-B (PI: Segal) 09/01/16 – 08/31/18
Foundation for Angelman Syndrome Therapeutics
FAST Integrative Research Environment (FIRE) Initiative
The goal of this project is to develop a therapy based on an artificial transcription factor (ATF) that can turn on the silenced paternal allele of UBE3A. The award provides support to staff in my laboratory.
Role on Project: *Co-investigator*

R01 HL124879 (MPI: Ferrara, Jo) 10/01/13 – 04/30/18
NIH/NCI
Image-based analysis of miRNA delivery
Project involves the development of miRNA delivery particles based on an analysis of native particles.

R01 CA134659 (PI: Ferrara) 05/17/09 – 03/31/18
NIH/NCI
Ultrasonic assessment of therapeutic response
The overall goal is to develop systemic immunotherapy using ultrasound using ablation and real-time methods to assess response to cancer therapy using ultrasound.