

BIOGRAPHICAL SKETCH

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NAME: **Katherine W. Ferrara**

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

POSITION TITLE: Interim Division Chief and 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 of lipid particles. My broad cross disciplinary training provides a unique foundation to accomplish the proposed work. 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 had 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 six societies spanning physics, biomedical and electrical engineering and imaging. My publications are indexed by ferrara k* and include more than 300 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. I am excited to work with the PI on the development of a COVID vaccine and can contribute to this project based on our work in imaging viral vectors and pseudoviruses.

1. Tali Ilovitsh, Elizabeth S. Ingham, Hua Zhang, Asaf Ilovitsh, Bo Wu, Brett Z. Fite, Yi Feng, Spencer K. Tumbale, Josquin Foiret, Azadeh Kheiriloom, Michael Chavez, Ophir Vermesh, Idan Steinberg, Sanjiv S. Gambhir, Gadi Pelled and **Ferrara KW**, Low frequency ultrasound-mediated cytokine transfection enhances T cell recruitment at local and distant tumor sites, Proc Natl Acad Sci U S A. 2020 Jun 9;117(23):12674-12685. doi: 10.1073/pnas.1914906117.
2. Jai Woong Seo, Elizabeth S. Ingham, Lisa Mahakian, Spencer Tumbale, Shahin Shams, Xiaozhe Ding, Nicholas Goeden, Tatyana Dobrava, Kratika Singhal, Michael Chavez, Ryan Leib, David Segal, Eduardo Silva, Viviana Gradinaru, **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, PMID 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.

- Bez M, Sheyn D, Tawackoli W, Avalos P, Shapiro G, Giaconi JC, Da X, David SB, Gavriity 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
2020-	Interim Division Chief, MIPS, Stanford University

Selected Experience and Professional Memberships

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, World Molecular Imaging Society

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

2012 IEEE Achievement Award (top award from IEEE ultrasonic society)

2014 Election to National Academy of Engineering

2017 IEEE Distinguished Lecturer in Ultrasonics

2019 Judith Poole Award from Association of Women in Science (for mentorship)

2019 Distinguished Investigator Award, Academy for Radiology & Biomedical Imaging Research

2019 Gold Medal, World Molecular Imaging Society

2020 2021 IEEE Biomedical Engineering Award

2020 IEEE Rayleigh Award

C. Contributions to Science (h index currently 71)

Enhanced immunotherapeutics

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

- 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.
- 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.
- 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, 2018 Sep 19. doi: 10.1039/c8bm00891d, PMC6261306.
- Silvestrini MT, Ingham ES, Liu Y, Fite BZ, Mahakian LM, Tam SM, Kheirilomoom 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.

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. Kheirloomoom 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, Skafnesmo 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.

13. Kheirloomoom 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, Kheirloomoom 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. Kheirloomoom 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.

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

<http://scholar.google.com/citations?user=7mTBiAQAAAAJ&hl=en>

D. Research Support

R01CA250557 (PI: Ferrara, MPI: Levy)

02/01/21-01/31/26

NIH/NCI

Imaging modulation of immune phenotype

Major Goals: The goal is to modulate and image T cell activation

1R01CA2533161 (PI: Ferrara)

07/01/20-06/30/25

NIH/NCI

HIFU-immunotherapy in pancreatic cancer

Major Goals: The goal is to develop a strategy combining ultrasound with the co-delivery of small molecule immune agonists encapsulated in temperature-sensitive particles in pancreatic cancer.

R01CA112356 (PI: Ferrara)

07/01/05 – 06/30/23

NIH/NCI

Insonation of ultrasound microbubbles at low frequency to enhance image-guided therapy

Major Goal: The objective of this project is to transfect tumors to produce components of suicide gene therapy protocols.

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 for liver imaging.

1R01EB028646 (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.

1R01EB028646S-01 (PI: Ferrara)

07/15/20 – 07/14/21

NIH/NIBIB

In vivo PET imaging of pseudotype viruses

The goal of this award is to investigate SARS-CoV-2 pseudotype viruses with imaging.

R01CA227687-01 (PI: Butts-Pauly)	03/01/18 – 02/28/23
NIH/NCI	
<i>The Impact of FUS-Mediated Brain Cancer Therapy on BBB Transport, Cytokines, and Immunocyte Trafficking</i>	
The goal is to assess the safety and efficacy of BBB transport as a function of ultrasound parameters.	
Role on Project: <i>Co-investigator</i>	
R01EB026094 (PI: Gazit)	04/01/18 – 03/31/22
NIH/NIBIB	
<i>Ultrasound-guided DNA delivery for regenerative medicine</i>	
The goal is to transfect stem cells to enhance healing of bone and ligaments.	
Role on Project: <i>Co-investigator</i>	
R01CA210553 (PI: Ferrara)	07/01/16 – 06/30/21
NIH/NCI	
<i>Image-guided ultrasound therapy and drug delivery in pancreatic cancer</i>	
We are developing a temperature-sensitive gemcitabine liposome and squalene-gemcitabine particles and developing MRgFUS methods for pancreatic cancer therapy.	
Focused Ultrasound Surgery Foundation (PI: Ferrara)	01/01/20 - 12/31/21
<i>αCD40 + Ablation trial</i>	
Single cell sequencing of pancreatic cancer treated with HIFU, checkpoint inhibitors, CD40 and the combination.	
Focused Ultrasound Foundation (PI: Ghanouni)	10/01/20 - 05/01/23
<i>MRgFUS ablation in human pancreatic cancer</i>	
We will conduct a human study of ablation combined with standard of care chemotherapy.	
Stanford Tübingen Grant (PI: Ferrara)	01/01/20 - 12/31/21
Internal funding: <i>Translational CD40 imaging</i>	
We focus on developing a joint program and building translational antibody imaging of the myeloid compartment.	
Stanford Bio-x grant (PIs: Ferrara and Qi)	10/01/20-9/30/22
<i>Harnessing ultrasound to control gene expression and editing</i>	
Major goal: Develop a method to control gene editing with ultrasound	
Stanford PHIND program (PI:Ferrara)	02/01/21-01/31/22
<i>Using photoacoustic imaging for the detection of new endogenous near-infrared biomarkers in high-risk atherosclerotic plaques</i>	
<u>Completed Research Support (past 3 years)</u>	
R01CA199658 (PI: Ferrara)	07/01/15 – 10/31/20
NIH/NCI	
<i>Optimized ultrasound-enhanced immunotherapy</i>	
Project involves the development of ultrasound thermometry and ultrasound-guided doxorubicin delivery with hyperthermia.	
6143-1089-03-B (PI: Segal)	09/01/16 – 08/31/18
Foundation for Angelman Syndrome Therapeutics	
<i>FAST Integrative Research Environment (FIRE) Initiative</i>	
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: <i>Co-investigator</i>	
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.	