

BIOGRAPHICAL SKETCH

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NAME: **Welch, Danny R.**

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

POSITION TITLES: **Professor of Cancer Biology | Associate Director - Cancer Education and Career Enhancement | Hall Family Endowed Professor of Molecular 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)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of California at Irvine	B.S.	09/1976	06/1980	Biological Sciences
University of Texas - Houston	Ph.D.	07/1980	05/1984	Biomed. Sci.-Tumor Biol.
University of Texas - M.D. Anderson Cancer Center	Postdoc	05/1984	08/1984	Tumor Biology - Metastasis

A. Personal Statement

I have studied various aspects of cancer biology, tumor progression and metastasis since I was a student at UCI. I was the first graduate student in the Dept. of Tumor Biology at M.D. Anderson Cancer Center, where I studied phenotypic and genetic instability leading to development of heterogeneity as well as developing aerosolized liposomal drug delivery methods under the tutelage of Garth Nicolson. Following graduate school I worked my way through the ranks in the discovery programs at Upjohn and Glaxo before taking a first faculty position at Penn State-Hershey Medical Center, where I was the first hire into the Jake Gittlen Cancer Research Institute. At Penn State, the focus of my research shifted to discovery of metastasis-regulatory genes. There we cloned 2 of the now >30 metastasis suppressors (KISS1 and BRMS1) and began to characterize their function(s). I was then recruited to UAB where my lab continued to define the regulatory pathways in mechanisms of action for these and an additional 4 metastasis suppressors and metastasis-regulatory microRNA. Since moving to the University of Kansas Cancer Center, we discovered two more metastasis suppressors and began shifting toward a more translational focus, applying our past genetics and epigenetics work to studying the roles of mitochondrial genetics in regulating complex diseases, focusing on metastasis. The major tumor types studied in my lab are breast, melanoma, pancreatic ductal adenocarcinoma, but I also have experience in colorectal, lymphoma, ovarian, bladder, prostate and neuroblastoma.

Research Expertise: My lab has published on a wide a breadth of topics as we have characterized the metastasis suppressors, including G-protein coupled receptors, phosphoinositide signaling, dormancy, chromatin, epigenetics, microRNA regulation/function and mitochondrial genetics. Thus, I have experience in genetics, epigenetics, protein and membrane biochemistry, molecular biology, mouse models, and cell biology.

Leadership & Teaching: I have served on the external advisory boards for numerous cancer center (CCSG) and T32 grants as well as not-for-profit research and educational foundations. I have been primary mentor for 23 graduate students and 41 postdoctoral fellows, all of whom have obtained research positions in cancer research in academia, industry and government. I have served on committees for >100 others. I have launched three graduate programs (Cancer Biology at PSU, UAB and KUMC; and at UAB, and an HHMI-funded Med-to-Grad program in translational research) and have broad managerial experience, including personnel development, budget preparation, communication, and leadership of multi-investigator programs. I have reviewed for numerous NIH and HHMI graduate programs in addition to service on the Board of Directors for the Cancer Biology Training Consortium (CABTRAC) as Treasurer and President. In those roles, I was the lead author on a white paper defining the criteria for education with NCI-designated cancer Centers ([PMC4681646](#)). I also served on the AACR Science

Education Committee as Co-chair of the subcommittee for post-doctoral researchers and as liaison with the AACR Associate Member Council. I am currently Associate Director for Cancer Education and Career Enhancement at the NCI-designated University of Kansas Comprehensive Cancer Center.

For this proposal: I will work closely with Dr. Rigoutsos to help design the mouse-focused tools and databases to maximize their usefulness for wet-bench scientists like me. I will also beta test these tools and databases. Dr. Rigoutsos and I will use the valuable information generated from this framework to carefully study functionality and mechanisms of action for specific mouse tRFs that we have identified as important through parallel work.

Ongoing and recently completed projects:

Sponsor: NIH (P30 CA168524)	07/01/2022 - 06/30/2027	Role: AD-Education
Project Title: Cancer Center Support Grant (PI: Jensen)		
Sponsor: NIH (R21CA277516)	02/01/2023 - 01/31/2025	Role: MPI
Project Title: Regulatory Role of Mitochondrial DNA in Bladder Cancer Progression		
Sponsor: Metavivor Research & Support	01/01/2020 - 2/28/2024	Role: PI
Project Title: New inhibitors of breast cancer metastasis		
Sponsor: Metavivor Research & Support	02/01/2023 - 01/31/2025	Role: PI
Project Title: Mitochondrial Modifiers of Metastasis		
Sponsor: Nat'l Fndn for Cancer Res	01/01/2018 - 01/30/2024	Role: PI
Project Title: NFCR Fellow - Welch		
Sponsor: DOD (W81XWH2110001)	09/30/2020 - 06/30/2023	Role: Co-investigator
Project Title: Subpopulations of Osteoblasts Are Present in the Bone-Tumor Niche During Bone Metastatic Breast Cancer		
Sponsor: ACS (PF-16-227-O1-CSM)	09/30/2016 - 06/30/2020	Role: Mentor
Project Title: Subpopulations of Osteoblasts Are Present in the Bone-Tumor Niche During Bone Metastatic Breast Cancer, Function and Regulation of the Metastasis Suppressor Domain of BRMS1 (PI: C. Manton)		
Sponsor: Komen (CCR18548252)	2018-2022	Role: Co-Mentor
Project Title: Chemo-Sensitization of Triple Negative Breast Cancer by Targeting HuR (PI: Xiaoqing "Sarah" Wu)		
Sponsor: NIH (F30CA216998)	2018-2021	Role: Mentor
Project Title: The role of ITIH5 in suppressing pancreatic cancer metastasis (PI: Eric Young)		
Sponsor: DOD (W81XWH-16-1-0730)	2016 - 2021	Role: PI
Project Title: Blocking breast cancer metastasis by modulation the RNA-binding protein HuR		
Sponsor: PCORI (6102.FE.20170816)	2018 - 2020	Role: MPI
Project Title: Metastasis Research Society•Metavivor Strategic Partnership for Metastatic Patient Outcomes - Eugene Washington Engagement Award		

B. Positions, Scientific Appointments and Honors

2011- now	<u>The University of Kansas Medical Center –</u>	
	2011-now	Professor & Founding Chair, Department of Cancer Biology Hall Family Foundation Professor of Molecular Medicine Professor: Pathology & Laboratory Medicine, Molecular & Integrative Physiology, Internal Medicine (Hematology/Oncology)
	2011-2017	Director - NFCR Center for Metastasis Research
	2016-2018	Director - Graduate Programs (MS/PhD) in Cancer Biology

	2014-2019	Faculty Director - Office of Postdoctoral Affairs <u>The University of Kansas Cancer Center</u> –
	2011-2018	Associate Director for Basic Research
	2014-now	Associate Director for Cancer Education and Career Development
2002-2011		<u>University of Alabama at Birmingham</u> –
	2002-2011	Leonard H Robinson Professor of Pathology Professor of Pharmacology & Toxicology Director - NFCR Center for Metastasis Research Senior Member, UAB O’Neal Comprehensive Cancer Center Senior Member, Center Metabolic Bone Disease Senior Member, Gene Therapy Center Senior Member, Skin Diseases Research Center
	2004-2011	Professor of Cell Biology
	2008-2011	Director, UAB Graduate Program in Cancer Biology Director’s Council, UAB O’Neal Comprehensive Cancer Center
	2009-2011	Director, Howard Hughes Med-to-Grad Graduate Program
1990-2002		<u>Penn State University College of Medicine</u> –
	1990-1997	Assistant Professor of Pathology
	1997-2003	Associate Professor of Pathology (tenured)
	1994-2003	Associate Professor of Pharmacology
	1991-2003	Graduate Faculty, Penn State University College of Medicine
	1999-2002	Director - NFCR Center for Metastasis Research
1988-1990		<u>Glaxo Research Laboratories</u> –
	1988-1989	Senior Scientist III Department of Chemotherapy
	1989-1990	Res. Investigator Department of Chemotherapy
1984-1988		<u>The Upjohn Company</u> –
	1984-1988	Scientist I, Cancer & Infectious Diseases Research
	1988-1988	Scientist II, Cancer & Infectious Diseases Research

External Advisory Boards (Partial)

	2023-now	Holden Comprehensive Cancer Center (P30-CA086862)
	2022-now	Hollings Comprehensive Cancer Center (P30-CA138313)
	2021-now	Winthrop P. Rockefeller Cancer Institute
	2020-now	Houston Methodist Research Cancer Center
	2020-now	Van Andel Institute Epigenetics Program (T32-CA251066)
	2018-now	University of Nebraska Eppley Cancer Center - Pancreatic Cancer Metastasis (PO1-CA217798)
	2018-now	Chair, P20-GM121322 (Tumor Microenvironment COBRE) - West Virginia Health Sciences Univ.
	2017-now	Partnership Steering Committee - Moffitt Cancer Center–Ponce School of Medicine U54-CA163068
	2017-now	Vanderbilt T32-CA119925 Integrated biological systems training in oncology
	2015-now	Wake Forest Baptist Comprehensive Cancer Center P30CA012197
	2011-now	University of Michigan (Rogel) Cancer Biology Graduate Program (T32-CA009676; 2014--> Chair)
	2020-2025	Rutgers Youth Enjoy Science (RUYES) Program (R25CA24778)
	2020-2024	University of Kansas Medical Center Research Institute Board of Directors - Research Committee and Research Properties Committee
	2019-2023	Rutgers Cancer Research Institute - External Advisory Board P30-CA072720
	2019-2022	Stony Brook Cancer Center
	2018-2019	University of Arizona Cancer Center - Chair, Integrated Cancer Scholars (ICS) Training Program
	2017-2023	Van Andel Institute Graduate School Board of Directors
	2017-2021	Houston Methodist Research Institute - Physical Sciences-Oncology Center, Center for Immunotherapeutic Transport Oncophysics (U54-CA210181)
	2014-2017	NCI-F Study Section
	2011-2014	American Cancer Society Extramural Research Advisory Council
	2010-2020	Roswell Park Comprehensive Cancer Center P30-CA016056 Cancer Genetics Program
	2010-2015	Susan G. Komen for the Cure Scientific Advisory Council
	2007-2010	Susan G. Komen for the Cure Review Panels (Chair 2007, 2009, 2010, 2011-2015)
	2005,2007	European Union Framework VI and VII review panels
	2004-2010	NIH Cancer Genetics Study Section (Chair 2008-2010)
	2004-2005	US Army Medical Research & Materiel Command, Breast Cancer Research Program Integration

2001-2019	Panel P30-GM103332 (Center for Protease Research COBRE) — North Dakota State University (2001-2006; Chair, 2007-2012; Chair, 2013-2019)
2000-2011	American Institute for Cancer Research Scientific Review Panel B
2000-2010	California Breast Cancer Research Program (Chair 2008-2010)
1997-2003	ACS Study Section - Carcinogenesis, Nutrition & Environment (Chair, 2003)
1992-2001	Medical Director At-Large, American Cancer Society Commonwealth Division

Editorial Boards (key leadership and present)

2004-2011	Editor-in-Chief, <i>Clin Exptl Metastasis</i>	2000-now	<i>Clinical & Experimental Metastasis</i>
2009-2023	Deputy Editor, <i>Cancer Research</i>	2001-now	<i>Cancer & Metastasis Reviews</i>
2011-2023	Deputy Editor, <i>Cancer Today</i>	2001-now	<i>Cancer Research</i>
2013-2020	Associate Editor, <i>J Molec Medicine</i>	2011-now	<i>Cancer Today</i>

Honors and Awards (Selected)

2020	University of Kansas Medical Center Research Investigator Award
2018	University of Kansas Cancer Center – Director's Award for Mentorship
2016	Reuben Lotan Distinguished Lectureship (M.D. Anderson Cancer Center)
2012	Hall Family Professorship in Molecular Medicine
2011	Kansas Bioscience Authority Eminent Scholar
2010-2019	Komen Scholar (Susan G. Komen for the Cure)
2009-2013	Director, Howard Hughes Medical Institute Med-into-Grad Graduate Program (UAB)
2008	Metastasis Research Society Paget-Ewing Award for Excellence in Metastasis Research
2008	UAB Dean's Award for Excellence in Mentoring
2006-2008	President, Metastasis Research Society (Board of Directors 1998-2014)
2003, 2009	UAB Molecular and Cellular Pathology Graduate Student Teaching Award
2001	American Cancer Society Chairman's Award for Outstanding Efforts in Cancer Control
1983	Sigma Xi Fellow of the National Foundation for Cancer Research University of Kansas Cancer Center – Director's Award for Basic Science

C. Contributions to Science

1. Discovered 8 of the 30 functionally defined metastasis suppressors

- a. Lee, J.-H., Miele, M.E., Hicks, D.J., Phillips, K.K., Trent, J.M., Weissman, B.E. and **Welch, D.R.** (1996) KiSS-1, A novel malignant melanoma metastasis-suppressor genes identified in chromosome 6-malignant melanoma microcell hybrids. *Journal of the National Cancer Institute* 88: 1731-1737. PMID: 8944003
- b. Seraj, M.J.*, Samant, R.S.*, Verderame, M.F., **Welch, D.R.** (2000) Functional evidence for a novel human breast carcinoma metastasis suppressor, BRMS1, encoded at chromosome 11q13 * Contributed equally to this work. *Cancer Research* 60: 2764-2769. PMID: 10850410
- c. Young, E.D., Manley, S.J., Beadnell, T.C., Shearin, A.E., Sasaki, K., Zimmermann, R., Kauffman, E., Vivian, C.J., Parasuram, A., Iwakuma, T., Grandgenett, P.M., Hollingsworth, M.A., O'Neil, **Welch, D.R.** (2020) Suppression of pancreatic cancer liver metastasis by secretion-deficient ITIH5. *British Journal of Cancer* 124, 166-175 PMID: 33024269 [PMC7782545](#).
- d. Zimmermann, R.C., Sardu, M.E., Manton, C.A., Miah, M.S., Banks, C.A., Adams, M.K., Koestler, D.C., Washburn, M.P., **Welch, D.R.** (2021) Perturbation of BRMS1 interactome reveals pathways that impact cell migration. *PLoS One* 16:e0259128. PMID: 34788285 [PMC8271116](#).

2. First to identify the pro-metastatic role for neutrophils (similar to myeloid-derived suppressor cells) and pro-invasive/pro-metastasis effect of TGFβ

- a. **Welch, D.R.**, Schissel, D.J., Howrey, R.P. & Aeed, P.A. (1989) Tumor-elicited polymorphonuclear cells, in contrast to 'normal' circulating polymorphonuclear cells, stimulate invasive and metastatic potentials of rat mammary adenocarcinoma cells. *Proceedings of the National Academy of Science (USA)* 86:5859-5863. PMID: 2762301
- b. **Welch, D.R.**, Fabra, A. & Nakajima, M. (1990) Transforming growth factor-beta stimulates mammary adenocarcinoma cell invasion and metastatic potential. *Proceedings of the National Academy of Science*

(USA) 87:7678-7682. PMID: 2217201

- c. McGary, C.T., Miele, M.E., **Welch, D.R.** (1995) Highly metastatic 13762NF rat mammary adenocarcinoma clones secrete IL-3 or GM-CSF-like activity that is apparently responsible for neutrophilia response. *American Journal of Pathology* 147: 1668-1681. PMID: 7495292
3. **Developed and characterized many widely used metastasis models; wrote key methods review to perform metastasis assays; and, defined the first iteration of the hallmarks of cancer metastasis**
 - a. **Welch, D.R.**, Bisi, J.E., Miller, B.E., Conaway, D., Seftor, E.A., Yohem, K.H., Gilmore, L.B., Seftor, R.E.B., Nakajima, M. & Hendrix, M.J.C. (1991) Characterization of a highly invasive and spontaneously metastatic human malignant melanoma cell line. *International Journal of Cancer* 47:227-237. PMID: 1671030
 - b. **Welch, D.R.** (1997) Technical considerations when studying cancer metastasis in vivo. *Clinical and Experimental Metastasis* 15(3): 272-306. PMID: 9174129
 - c. **Welch, D.R.**, Lobl, T.J., Seftor, E.A., Wack, P.J., Aeed, P.A., Yohem, K.H., Seftor, R.E.B. & Hendrix, M.J.C.(1989) Use of the membrane invasion culture system (MICS) as a screen for anti-invasive agents. *International Journal of Cancer* 43:449-457. PMID: 2925275
 - d. **Welch, D.R.**, Hurst, D.R. (2019) Defining the Hallmarks of Metastasis. *Cancer Research* 79:3011-3027 (doi: 10.1158/0008-5472.CAN-19-0458) PMID: 31053634; [PMC6571042](#)
4. **Defined the first molecular pathways regulating metastasis and metabolism (includes microRNA) and how KISS1 induces dormancy of already disseminated cells and regulates metabolism**
 - a. Nash, K.T., Phadke, P.A., Navenot, J.-M., Hurst, D.R., Accavitti-Loper, M.A., Sztul, E., Vaidya, K.S., Frost, A.R., Kappes, J.C., Peiper, S.C. and **Welch, D.R.** (2007) KISS1 metastasis suppressor secretion is required for multiple organ metastasis suppression and for the maintenance of disseminated cells in a dormant state. *Journal of the National Cancer Institute* 99: 309-321. (DOI:10.1093/jnci/djk053) PMID: 17312308 [PMC1820615](#)
 - b. Hurst, D.R., Edmonds, M.D., Scott, G.K., Benz, C.C. and **Welch, D.R.** (2009) Breast cancer metastasis suppressor 1 BRMS1 up-regulates miR-146 that suppresses breast cancer metastasis. *Cancer Research* 69: 1279-1283 (DOI:10.1158/0008-5472.CAN-08-3559) PMID: 19190326.
 - c. Liu, W., Beck, B.H., Vaidya, K.S., Nash, K.T., Feeley, K.P., Ballinger, S.W., Pounds, K.M., Denning, W.L., Diers, A.R., Landar, A., Dhar, A., Iwakuma, T., **Welch, D.R.** (2014) Metastasis suppressor KISS1 seems to reverse the Warburg effect by enhancing mitochondrial biogenesis. *Cancer Research* 74: 954-963 (doi: 10.1158/0008-5472.CAN-13-1183) PMID: 24351292; [PMC3946400](#).
 - d. Young, E.D., Manley, S.J., Beadnell, T.C., Shearin, A.E., Sasaki, K., Zimmermann, R., Kauffman, E., Vivian, C.J., Parasuram, A., Iwakuma, T., Grandgenett, P.M., Hollingsworth, M.A., O'Neil, **Welch, D.R.** (2020) Suppression of pancreatic cancer liver metastasis by secretion-deficient ITIH5. *British Journal of Cancer* 124, 166-175 (doi: 10.1038/s41416-020-01093-z) PMID: 33024269 [PMC7782545](#).
5. **Developed the MNX mouse to study cross-talk between mitochondrial and nuclear DNA for the study of cancer, cardiovascular disease and other complex diseases. Defined mitochondrial QTL.**
 - a. Feeley, K.P., Bray, A.W., Westbrook, D.G., Johnson, L.W., Kesterson, R.A., Ballinger, S.W. **Welch, D.R.** (2015) Mitochondrial genetics regulate breast cancer tumorigenicity and metastatic potential. *Cancer Research* (doi: 10.1158/0008-5472.CAN-15-0074) 75(20):4429-36. [PMC4610037](#)
 - b. Vivian, C.J., Brinker, A.E., Graw, S., Koestler, D.E., Legendre, C., Gooden, G., Salhia, B., **Welch, D.R.** (2017) Mitochondrial genomic backgrounds affect nuclear DNA methylation and gene expression. *Cancer Research* (doi: 10.1158/0008-5472.CAN-17-1473) 99(22): 6202-14. PMID: 28663334 [PMC5690839](#).
 - c. Brinker, A.E., Vivian, C.J., Beadnell, T.C., Koestler, D.C., Teoh, S.T., Lunt, S.Y., **Welch, D.R.** (2020) Mitochondrial haplotype of the host stromal microenvironment alters metastasis in a non-cell autonomous manner. *Cancer Research* 80(5): 1118-1129 (doi: 10.1158/0008-5472.CAN-19-2481) PMID: 31848195 [PMC7056497](#).
 - d. Beadnell, T.C., Fain, C., Vivian, C.J., King, J.C., Hastings, R., Markiewicz, M.A., **Welch, D.R.** (2020) Mitochondrial genetics appear to alter immune cell development/trafficking. *Biochimica et Biophysica Acta - Molecular Basis of Disease* 1866(5):165648 (doi: 10.1016/j.bbdis.2019.165648) PMID: 31899295 [PMC7071984](#).

Complete List of Published Work in MyBibliography:

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