

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME Danny R. Welch		POSITION TITLE Leonard H. Robinson Professor of Pathology Professor of Cell Biology and Pharmacology/Toxicology	
eRA COMMONS USER NAME DWELCH			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California at Irvine	B.S.	1980	Biological Sciences
University of Texas - Houston	Ph.D.	1984	Biomed. Sci.-Tumor Biol.
University of Texas - M.D. Anderson Cancer Center	Postdoc	1984	Tumor Biology - Metastasis

A. Positions and Honors

Upjohn Co: Scientist I (8/84-6/88); Scientist II (7/88-10/88) Dept of Cancer & Infect Dis Res
Glaxo, Inc: Sr Scientist III (10/88-10/89) Res. Investigator (10/89-5/90) Dept of Chemotherapy
Penn State College of Medicine: Asst Prof (11/90-06/97); Assoc Prof (7/97-10/03); Tenure (07/99) Dept Pharmacology; Assoc Prof (02/02-10/02); Director - Penn State-Natl. Fndn. Cancer Res. Ctr for Metastasis Res (10/01-10/02); Adj Assoc Prof of Pathology (11/02-06/03); Graduate Faculty (11/91-06/03)
U. Alabama - Birmingham: Sr Member - Cancer Ctr, Ctr Metabolic Bone Disease, Gene Therapy Ctr. (11/02-present); Graduate Faculty (11/02-present); Director, NFCR Ctr for Metastasis Res. (11/02-present); Dean's Award for Excellence in Mentoring (2008)
Awards/Honors: ACS PA-Division Chairman's Award for Outstanding Efforts in Cancer Control (2000)
Metastasis Research Society Paget-Ewing Award (2008)
University of Texas - Houston Distinguished Alumnus 2008-2009

Study Sections and Other Professional Activities (selected)

NCI – Cancer Genetics (CG; ad hoc 2004-5, Charter 2006-08, Chair, 2008-2010); multiple *ad hoc*.
ACS – Carcinogenesis, Nutrition & Environment (1997-2003; Chair 2003); Medical Director-at-Large, American Cancer Society – Pennsylvania Division (1992-2001)
USAMRMC – Breast & Prostate Cancer Panels (1995-2003; 2006); Integration Panel (2004-2005)
European Union - Framework VI (2005) and Framework VII (2007); Review and Consensus Panels
Misc – CA Cancer Res— Biomed. C (Chair 2000, 2002) Basic Breast Biol. (2000-5; 2007, Chair 2008); NJ Cancer Comm. (2000-2004), Susan Komen (Chair 2007; Integration Panel 2007), Am. Inst. Cancer Res (2000-8), Breast Cancer Canada (2000, 2002, 2004), Netherlands, Italian, Israel, CRC-UK Cancer Fndns
Editorial Boards (Current): *Cancer Res.*, *Cancer & Metastasis Rev.*, *Clin. Exptl. Metastasis*, *J. Mamm. Gland Biol. Neopl.*, *Curr. Cancer Ther.*, *J. Ovarian Res.*, *Hum. Carcinogenesis*, *Mol. Cancer Ther.*
Editor-in-Chief: *Clinical and Experimental Metastasis*, *Cancer Research Reviews* Section Editor

B. Selected peer-reviewed publications. Total—139 Peer-reviewed; 238 abstracts; 21 chapters; Editor 3 books):

Goldberg, S.F., (5 authors) and **Welch, D.R.** (2003) Melanoma metastasis suppression by chromosome 6: Evidence for a pathway regulated by DRIP130/CRSP3 and VDUP1. *Cancer Res* 63:432-440.
Harms, J.F. and **Welch, D.R.** (2003) MDA-MB-435 human breast carcinoma metastasis to bone. *Clin Exptl Met* 19: 327-334.
Shevde-Samant, L.A. and **Welch, D.R.** (2003) Metastasis suppressor pathways – an evolving paradigm. *Cancer Letters* 198: 1-20.
Mastro, A., Gay, C. and **Welch, D.** (2003) The skeleton as a unique environment for breast cancer cells. *Clin Exptl Met* 19: 3: 275-284.
Hunter, K., **Welch, D.R.** and Liu, E. (2003) Genetic background is a major determinant of metastatic potential. *Nature Genetics* 34: 23-24.
Mastro, A.M., Gay, C.V., **Welch, D.R.**, (5 authors) (2004) Breast cancer cells induce osteoblast apoptosis: a possible contributor to bone degradation. *J. Cellular Biochem* 91: 265-276.

- Meehan, W.J., Samant, R.S., (6 authors) & **Welch, D.R.** (2004) Interaction of the BRMS1 metastasis suppressor with RBP1 and the mSin3 histone deacetylase complex. *J Biol Chem* 279: 1562-1569.
- Lugassy, C., Kleinman, H.K., Engbring, J.A., **Welch, D.R.**, Harms, J.F., Rufner, R., Fernandez, P.M., Patierno, S.R., and Barnhill, R.L. (2004) Pericyte-like location of GFP melanoma cells: *Ex vivo* and *in vivo* studies of extravascular migratory metastasis. *Am J Pathology* 164: 1191-1198.
- Harms, J.F., **Welch, D.R.**, (28 authors) Griggs, D.W., (2004) A small molecule antagonist of the $\alpha_v\beta_3$ integrin suppresses MDA-MB-435 skeletal metastasis. *Clin Exptl Met* 21: 119-128.
- Kapoor, P., (6 authors), **Welch, D.R.** and Donahue, H.J. (2004) Breast cancer metastatic potential: Correlation with increased heterotypic gap junctional intercellular communication between breast cancer cells and osteoblastic cells. *Intl J Cancer* 111: 693-697 (10.1002/ijc.20318).
- Cicek, M., Samant, R.S., Kinter, M., **Welch, D.R.** and Casey, G. (2004) Identification of metastasis-associated proteins through protein analysis of metastatic MDA-MB-435 and metastasis-suppressed BRMS1-transfected MDA-MB-435. (2004) *Clin Exptl Met* 21: 149-157.
- Erin, N., (3 authors) and **Welch, D.R.** (2004) Capsaicin-mediated denervation of sensory neurons promotes mammary tumor metastasis to lung and heart. *Anticancer Res* 24: 1003-1010.
- Sadlonova, A., (5 authors), **Welch, D.R.**, and Frost, A.R. (2005) Primary breast fibroblasts modulate epithelial cell proliferation in three-dimensional *in vitro* co-culture. *Breast Cancer Res* 7:R46-R59.
- DeWald, D.B., (5 authors), **Welch, D.R.** (2005) Metastasis suppression by BRMS1 involves reduction of phosphoinositide signaling in MDA-MB-435 breast carcinoma cells. *Cancer Res* 65: 713-717.
- Cicek, M., Fukuyama, R., **Welch, D.R.**, Sizemore, N., Casey, G. (2005) Breast cancer metastasis suppressor (BRMS1) inhibits gene expression by targeting NF κ B activity. *Cancer Res* 65: 3586-3595.
- Koblinski, J.E., (9 authors), **Welch, D.R.**, Kleinman, H.K. (2005) Endogenous osteonectin/ SPARC/ BM-40 expression inhibits MDA-MB-231 breast cancer cell metastasis. *Cancer Res* 65: 7370-7377.
- Samant, R.S., Debies, M.T., Hurst, D.R., Moore, B.P., Shevde, L.A. and **Welch, D.R.** (2006) Suppression of murine mammary carcinoma metastasis by the murine ortholog of Breast Cancer Metastasis Suppressor 1 (*Brms1*). *Cancer Letters* 235: 260-265. doi:10.1016/j.canlet.2005.04.032. Published online 07/2005.
- Nash, K.T. and **Welch, D.R.** (2006) The KISS1 metastasis suppressor: mechanistic insights and clinical utility. *Frontiers in Bioscience* 11: 647-659 PMID: PMC1343480.
- Richert, M.M., (7 others) and **Welch, D.R.** (2005) Metastasis of hormone-independent breast cancer to lung and bone is decreased by -difluoromethylornithine treatment. *Breast Cancer Res* 7: R819-R827. PMID: PMC1242150
- Phadke, P.A., (11 others) and **Welch, D.R.** (2006) Kinetics of metastatic breast cancer cell trafficking in bone. *Clin Cancer Res* 12: 1431-1440. PMID: PMC1523260.
- Lugassy, C., Vernon, S.E., Busam, K., Engbring, J.A., **Welch, D.R.**, Poulos, E.G., Kleinman, H.K., and Barnhill, R.L. (2006) Angiotropism of human melanoma: Studies involving *in transit* and other cutaneous metastases and the chicken chorioallantoic membrane. Implications for extravascular melanoma invasion and metastasis. *Am J Dermatopathology* 28: 187-193. PMID: PMC1524855
- Shevde, L.A., (6 others) and **Welch, D.R.** (2006) Osteopontin knockdown suppresses tumorigenicity of human metastatic breast carcinoma. *Clin Exptl Metastasis* 23: 123-133. PMID: PMC1574364
- Mukherjee, S., (5 others), **Welch, D.R.**, (3 others) and Frost, A.R. (2006) Hedgehog signaling and response to cyclopamine differs in epithelial and stromal cells in benign breast and breast cancer. *Cancer Biol Ther* 5: 674-683. PMID: PMC1557635
- Rinker-Schaeffer, C.W., O'Keefe, J.P., **Welch, D.R.**, Theodorescu, D. (2006) Metastasis suppressor proteins: Discovery, molecular mechanisms and clinical application. *Clin Cancer Res* 12: 3882-3889. PMID: PMC1525213
- Hurst, D.R., (8 others), **Welch, D.R.**, and Samant, R.S. (2006) Breast cancer metastasis suppressor 1 (BRMS1) is stabilized by the Hsp90 chaperone. *Biochem Biophys Res Comm* 348: 1429-1435 PMID: PMC1557677
- Hicks, D.G., (15 others), **Welch, D.R.** and Casey, G. (2006) Loss of BRMS1 protein expression predicts reduced disease-free survival in a hormone receptor negative and HER2 positive subsets of breast cancers. *Clin Cancer Res* 12: 6702-6708. PMID: PMC1661839

- Sadlonova, A., (5 others), **Welch, D.R.**, Novak, L., and Frost, A.R. (2007) Human breast fibroblasts inhibit growth of the MCF10AT xenograft model of proliferative breast disease. *Am J Pathology* 170: 1064-1076. PMCID: PMC1864888
- Samant,R.S., (7 others), **Welch,D.R.**, Shevde,L.A. (2007) Breast cancer metastasis suppressor 1 (BRMS1) suppresses osteopontin by recruiting HDAC3 to a novel NF B site in the osteopontin promoter. *Mol Cancer* 16: 6:6 PMCID: PMC1796551
- Nash,K.T., (9 others) 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. *J Natl Cancer Inst* 99: 309-321. PMCID: PMC1820615
- Welch,D.R.** (2007) Do we need to redefine cancer metastasis and staging definitions? *Breast Disease: Metastasis*, Eds: L. Wakefield and K. Hunter, 26: 3-12. PMCID: PMC1868449
- Vaidya,K.S. and **Welch, D.R.** (2007) Metastasis suppressors and their roles in breast carcinoma. *J Mammary Gland Biol Neopl* 12: 175-190 PMCID: PMC1971219
- Cowin,P. and **Welch,D.R.** (2007) Breast cancer progression: controversies and consensus in the molecular mechanisms of metastasis and EMT. *J Mammary Gland Biol Neopl* . 12: 99-102 PMCID: PMC1963418
- Lugassy,C., Kleinman,H.K., Vernon,S.E., **Welch,D.R.** and Barnhill,R.L. (2007) C16 laminin peptide increases angiogenic extravascular migration of human melanoma cells in a shell-less chick CAM assay. *Br J Dermatol* 157: 780-782 PMID: 17711523
- Eccles,S.A. and **Welch,D.R.** (2007) Metastasis: recent discoveries and novel therapeutic strategies. *The Lancet* 369: 1742-1757. PMCID: PMC2214903
- Champine,P.J., Michaelson,J., Weimer,B.C., **Welch,D.R.** and DeWald,D.B. (2007) Microarray analysis reveals potential mechanisms of BRMS1 mediated metastasis suppression. *Clin Exptl Metastasis*. 24: 551-565. PMCID: PMC2214901
- Hurst,D.R. and **Welch,D.R.** (2007) A MSCing link in metastasis? *Nature Medicine (News & Views)* 13: 1289-1291. PMCID: PMC2267025
- Kapoor,P., Suva,L.J., **Welch,D.R.** and Donahue,H.J. (2008) Osteopontin and the bone metastatic potential of breast cancer cells. *J Cell Biochem* 103: 30-41. PMID: 17471510
- Phadke,P.A., Vaidya,K.S., Nash,K.T., Hurst,D.R., and **Welch,D.R.** (2008) BRMS1 suppresses breast cancer experimental metastasis to multiple organs by inhibiting several steps of the metastatic process. *Am J Pathology* 172: 809-817 PMCID: PMC2258257
- Bodenstine,T.M. and **Welch,D.R.** (2008) Metastasis suppressors and the tumor microenvironment. *Cancer Microenvironment* 1(1): 1-11 (doi: 10.1007/s12307-008-0001-8).
- Hurst, D.R., (7 others), & **Welch,D.R.** (2008) BRMS1:ARID4A direct interaction is required for transcription repression but not metastasis suppression. *J Biol Chem* 283: 7438-7444 PMCID: PMC2293288
- Stafford,L.J., Vaidya,K.S. and **Welch,D.R.** (2008) Metastasis suppressors genes in cancer. *Intl J Biochem Cell Biol* 40: 874-891 PMID: 18280770
- Hedley,B.D., **Welch,D.R.**, Allan,A.L., Al-Katib,W., Dales,D.W., Postenka,C.O., Casey,G., MacDonald,I.C., Chambers,A.F. (2008) Re-expression of osteopontin in breast cancer metastasis suppressor-1 expressing breast cancer cells restores metastatic potential. *International Journal of Cancer* 123(3):526-34 (doi: 10.1002/ijc.23542) PMID: 18470911
- Metge,B.J., Frost,A.R., King,J.A., Dyess,D.L., **Welch,D.R.**, Samant,R.S. and Shevde,L.A. (2008) Epigenetic silencing contributes to the loss of BRMS1 expression in breast cancer. *Clinical and Experimental Metastasis*. (10.1007/s10585-008-9187-x).
- Vaidya,K.S., Harihar,S., Phadke,P.A., Stafford,L.J., Hicks,D.G., Casey,G., DeWald,D.B. and **Welch,D.R.** (2008) Breast Cancer Metastasis Suppressor-1 differentially modulates growth factor signaling. *Journal of Biological Chemistry* (doi/10.1074/jbc.M710068200) PMID: 18664570
- Welch, D.R.**, Cooper, C.R., Hurst, D.R., Lynch, C.C., Martin, M.D., Vaidya, K.S., VanSaun, M.N., and Mastro, A.M. Metastasis Research Society- American Association for Cancer Research Joint Conference on Metastasis. *Cancer Research* (In press)
- Hurst, D.R., Xie, Y., Edmonds, M.D., Welch, D.R. (2008) Multiple forms of BRMS1 are differentially expressed in the MCF10 isogenic breast cancer progression model. *Clinical and Experimental Metastasis* (10.1007/s10585-008-9216-9). PMID: 18841483.

C. Research Support.

ACTIVE

5R01 CA87728-09 (Welch) 07/01/00 - 04/30/09
PHS/NCI
Molecular Regulation of Breast Cancer Metastasis
Goals: Biochemical characterization of BRMS1, a human breast cancer metastasis suppressor gene

No Identifying Number (Welch) 10/01/95 - 09/30/10
National Foundation for Cancer Research
NFCR Center for Metastasis Research
Goals: Multi-investigator, multi-institutional team studying metastasis. NFCR-CMR provides funding for seed grants. Initial studies focus on bone and melanoma metastasis.

W81-XWH-07-1-0399 (Welch) 07/01/07 - 06/30/10
Department of Defense - Idea
Treatment strategy to reverse osteolytic breast cancer metastasis using osteoblasts
Goals: To engineer apoptosis-resistant stem cells to repair osteolytic breast cancer metastasis

R13 CA110143-02 (Welch) 09/01/04 - 08/31/09
PHS/NCI
International Congresses - Metastasis Research Society

R01 CA84248 (S. Bellis, Welch - Co-PI) 10/01/07 - 09/30/12
Regulation of beta1 integrin glycosylation by ras

COMPLETED (within past 3 yr)

DAMD17-02-1-0541 (Welch) 05/31/02 - 06/30/06
Department of Defense - Idea
Metastasis Genes in Breast Cancer to Bone

P50 CA83591 (Partridge) 02/01/06 - 09/30/06
PHS/NCI

SPORE in Ovarian Cancer. Pilot Project: Metastasis suppressors in ovarian cancer

P50 CA89019 (Bland) 10/01/03 - 09/30/06

PHS/NCI

SPORE in Breast Cancer. Project #2 (Project Director): Molecular Regulation of Breast Cancer Metastasis

PDF122006 (Welch) 05/01/06 - 04/30/08

Susan G. Komen Breast Cancer Foundation

BRMS1 modulation of EGF-receptor signaling Goals: Postdoctoral Mentor for Kedar S. Vaidya, Ph.D.

Study #1 (Welch) 01/01/2008 - 04/30/2008

Chemokine Therapeutics Inc,

Assessment of CTCE-9908 as breast cancer anti-metastatic agent

F32 CA113037-01 (Welch) 09/01/05 - 08/31/08

PHS/NCI

Mechanistic insight into BRMS1 metastasis suppressor

Goals: Postdoctoral training - Douglas R. Hurst, Ph.D.

BC063079 (Ballinger, Welch - Co-PI) 10/01/2007 - 07/31/2008

Department of Defense - Concept

Mitochondrial-nuclear compatibility in metastatic susceptibility