

BIOGRAPHICAL SKETCH

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NAME Robert Clarke, Ph.D., D.Sc.	POSITION TITLE		
eRA COMMONS USER NAME: Bob_Clarke	Professor of Oncology, Physiology & Biophysics Associate Vice President, GUMC		
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Ulster University, Jordanstown, Co. Antrim, U.K.	B.Sc.	1980	Biological Sciences
Queen's University of Belfast, N. Ireland, U.K.	M.Sc.	1982	Biochemistry
Queen's University of Belfast, N. Ireland, U.K.	Ph.D.	1986	Biochemistry
Medicine Branch, N.C.I., N.I.H., Bethesda, MD, U.S.A.	Postdoc	1987-1988	Breast Cancer
Queen's University of Belfast, N. Ireland, U.K.	D.Sc.	1999	Biochemistry

Research and Professional Experience

1989-91 Research Assistant Professor, Dept. Physiology & Biophysics, Georgetown University Medical Center (GUMC)
1989-2007 Director, Lombardi Cancer Center Animal Research Resource, Georgetown University
1991-95 Assistant Professor (tenure track), Dept. Physiology & Biophysics, Georgetown University
1995-98 Associate Professor (with tenure), Dept. Physiology & Biophysics, Georgetown University
1999-date Professor (with tenure), Depts. Oncology and Physiology & Biophysics, Georgetown University
2005-date Chair, Division of Molecular Endocrinology, Nutrition and Obesity, Georgetown University (GUMC)
2006-date Co-Director, Breast Cancer Program, Lombardi Comprehensive Cancer Center, GUMC
Member Am Assoc Cancer Res, Am Assoc Adv Sci, Am Chem Soc, Endocrine Society, NY Acad Sci

Study Section/Grant & Manuscript Reviews (partial listing)

1993, 2006 *Ad hoc* member, N.C.I. Board of Scientific Advisors
1995-date Member, several N.I.H. Program Project (P01) and S.P.O.R.E. Review Panels
1995-2005 Chair, 1998, 2005; Member, DOD Study Section - *Clinical & Experimental Therapeutics-1*
1996-date *Ad hoc* member, multiple N.I.H. Study Sections, e.g., *Experimental Therapeutics-1; Medical Biochemistry; Metabolic Pathology; Basic Mechanisms of Cancer Therapeutics*
1998-2002 Member, N.I.H. Oncological Sciences Study Section: *SEP ZRG2 SSS-1 (SBIR/STTR)*
2007, 2008 *Ad hoc* member, *Integration Panel* (Breast Cancer Research Program, Department of Defense)
2002-2008 Chair, N.I.H. Study Section: *Basic Science - ZAT1 DB1 (NCCAM)*
2008, 2009 Chair, DOD Study Section - *Cell Biology-3*
2007-2009 Chair, State of Nebraska Technical Review Panel "*Cancer and Smoking Disease Research*"
Manuscripts reviewed multiple journals, e.g., *Science, Cancer Cell, Proc Natl Acad Sci, J Clin Invest, JNCI*

Editorial Boards and Program Committees (selected)

1992-date Member, Editorial Advisory Board, *Breast Cancer Research and Treatment*
1997-date Member, Editorial Board, *British Journal of Cancer*; Member, Editorial Board, *Oncology Reports*
1997 Chairperson, *Clinical Endocrinology*, AACR Program Committee: 89th Annual AACR Meeting
1998 Member, *Experimental Therapeutics*, AACR Program Committee: 90th Annual AACR Meeting
2000 Co-Chairperson, Conference: Nutrition in Preventing and Treating Breast & Prostate Cancer
2002-date Member, Editorial Board, *Journal of Steroid Biochemistry and Molecular Biology (JSBMB)*
2003-date Member, Editorial Board, *Cancer Genomics and Proteomics*
2004, 2008 Member, Program Committees *7th and 8th International Conference of Anticancer Research*
2005-date Member, Editorial Academy, *International Journal of Oncology*
2006-date Member, Editorial Boards, *Clinical Cancer Research and Molecular Cancer Therapeutics*
2008-date Member, Editorial Board, *Cancer Prevention Research*
2007-date Senior Editor, *Cancer Research* (Associate Editor, 2001-2007)

Awards/Honors/Patents/Other (selected)

1987-88 N.C.I. Breast Cancer Study Group Fellowship, Medicine Branch, N.I.H.
1997 Fellow: elected, *Royal Society of Chemistry* (FRSChem) and *Royal Society of Biology* (FSBiol; UK)
2000 100 most published breast cancer researchers; 23rd San Antonio Breast Cancer Symp
2001 Fellow (elected), *Royal Society of Medicine* (FRSMed; UK)
2007 Arnold Greenberg Distinguished Lectureship, Institute of Cell Biology, University of Manitoba
2007 Distinguished Lectureship, University of Texas Health Sciences Center at San Antonio
Patents U.S. Patent 5,091,423 (1992); U.S. Patent 08/667,542 (1997)

Sessions chaired at recent conferences – *18th Intl Symp JSBMB* (2008); *caBIG Joint Architecture/Vocabularies and Data Elements Workspaces* (2007); *N Am Res Conf Compl Med* (2006); *DOD BCRP Era of Hope* (2005).

Relevant Publications: from a total of >200 publications and 10 submitted manuscripts.

1. Crawford AC, Riggins RB, Shajahan AN, Zwart A, **& Clarke R.** BCL-W and BCL2 are key regulators of apoptotic, necrotic and autophagic cell fate in response to antiestrogens. *PLoS ONE*, 5 (1): e8604, 2010.
 2. Zhang Y, Xuan J, de los Reyes BG, **Clarke R** & Resson HW. Reconstruction of gene regulatory modules in cancer cell cycle by multi-source data integration. *PLoS ONE*, 5 (4): e10268, 2010.
 3. Ning Y, Riggins RB, Mulla JE, Chung H, Zwart A & **Clarke R.** IFN γ restores breast cancer sensitivity to Fulvestrant by regulatinh STAT1, IRF1, NFkB, BCL2, and signaling to caspase-dependent apoptosis. *Mol Cancer Ther*, 9: 1274-85, 2010 (featured on journal cover).
 4. Nehra R, Riggins RB, Shajahan AN, Zwart A, Crawford AC **& Clarke R.** BCL2 and CASP8 regulation by NFkB affect mitochondrial function and cell fate in antiestrogen sensitive and resistant breast cancer cells. *FASEBJ*, 24: 2039-2054, 2010.
 5. Chen L, Xuan J, Riggins RB, Wang Y, Hoffman EP **& Clarke R.** Multi-level support vector regression analysis to identify condition-specific regulatory networks. *Bioinformatics*, in press.
 6. **Clarke R.** Shajahan AN, Riggins RB, Cho Y, Crawford A, Xuan J, Wang Y, Zwart A, Nehra R & Liu MC Gene network signaling in hormone responsiveness modifies apoptosis and autophagy in breast cancer cells. *J Steroid Biochem Mol Biol*, 114:8-20, 2009.
 7. **Clarke R.** Resson H, Wang A, Xuan J, Liu, MC, Gehan E. & Wang Y. Properties of high dimensional data spaces: implications for exploring gene and protein expression data. *Nature Rev Cancer*, 8:37-49, 2008.
 8. Riggins RB, Lan J, Klimach U, Zwart A, Cavalli LR, Haddad BR, Xuan J, Ethier SP **& Clarke, R.** ERR γ mediates Tamoxifen resistance in invasive lobular carcinoma. *Cancer Res*, 68:8908-8917, 2008 (featured in journal *Highlights* section).
 9. Shajahan A, Wang A, Decker M, Minshall RD, Liu, MC **& Clarke R.** Caveolin-1 tyrosine phosphorylation (Y14) enhances paclitaxel-mediated cytotoxicity. *J Biol Chem*, 282: 5934-5943, 2007.
 10. Gomez BP, Riggins RB, Klimach U, Zhu Y, Zwart A, Wang M, Wang A **& Clarke R.** X-box binding protein-1 confers estrogen-independence and antiestrogen resistance in breast cancer. *FASEBJ*, 21:4013-27, 2007.
 11. Wang LH, Yang XY, Zhang X, An P, Kim H-J, Huang J, **Clarke, R.** Osborne CK, Inman JK, Appella E & Farrar WL. Disruption of estrogen receptor DNA-binding domain and related intramolecular communication restores tamoxifen sensitivity in resistant breast cancer. *Cancer Cell*, 10: 487-499, 2006.
 12. Trock BJ, Hilakivi-Clarke LA **& Clarke R.** Meta-analysis of soy intake and breast cancer risk. *J Natl Cancer Inst*, 98:459-471, 2006 (subject of Editorial).
 13. Bouker KB, Skaar TC, Fernandez DR, O'Brien KA, **& Clarke R.** Interferon regulatory factor-1 mediates the proapoptotic but not cell cycle arrest effects of ICI 182,780. *Cancer Res*, 64:4030-4039, 2004.
 14. Johnson M, Kenney N, Hilakivi-Clarke L, Singh S, Chepko G, Newbold R, **Clarke R.** Sholler PF, Lirio AA, Foss C, Trock B, Paik S, Stoica A & Martin MB. Cadmium mimics the effects of estrogen *in vivo* in the uterus and mammary gland. *Nature Med*, 9:1081-1084, 2003.
 15. Pratt MAC, Bishop TE, White D, Yasvinski G, Ménard M, Niu MY **& Clarke R.** Estrogen withdrawal-induced NFkB and Bcl-3 expression in breast cancer hormone independence. *Mol Cell Biol*, 23:6887-6900, 2003.
 16. Gu Z, Lee RY, Skaar TC, Bouker KB, Welch JN, Lu J, Liu A, Davis N, Leonessa F, Brünner N, Wang Y **& Clarke R.** Association of interferon regulatory factor-1, nucleophosmin, nuclear factor-kB and cAMP response element binding with resistance to Faslodex (ICI 182,780). *Cancer Res*, 62:3601-3610, 2002.
 17. Arteaga CL, Koli KM, Dugger TC **& Clarke R.** Reversal of tamoxifen resistance in human breast cancer cells *in vivo* with neutralizing anti-TGF β antibodies. *J Natl Cancer Inst*, 91:46-53, 1999.
 18. Hilakivi-Clarke LA, **Clarke R.** Onojafe I, Raygada M, Cho E & Lippman, ME. A maternal diet high in n-6 polyunsaturated fats alters mammary gland development, puberty onset, and breast cancer risk among female rat offspring. *Proc Natl Acad Sci USA*, 94:9372-9377, 1997.
 19. Trock B, Leonessa F **& Clarke R.** Multidrug resistance in breast cancer: meta analysis of MDR1 expression and its possible functional significance. *J Natl Cancer Inst*, 89:917-931, 1997 (subject of two Editorials).
 20. Brünner N, Boysen B, Jirus S, Skaar TC, Holst-Hansen C, Lippman J, Frandsen T, Spang-Thomsen M. Fuqua SAW **& Clarke R.** MCF7/LCC9: antiestrogen resistant MCF-7 variant where acquired resistance to ICI 182,780 confers early crossresistance to Tamoxifen. *Cancer Res*, 57:3486-3493, 1997.
 21. Leonessa F, Jacobson M, Boyle B, Lippman J, McGarvey M **& Clarke R.** Effect of tamoxifen on the breast cancer MDR phenotype: isobologram, accumulation and binding studies. *Cancer Res*, 54:441-447, 1994.
 22. Brünner N, Boulay V, Fojo A, Freter C, Lippman ME **& Clarke R.** Hormone-independence is accompanied by increased expression of E2-regulated genes but not DNA amplification. *Cancer Res*, 53:283-290, 1993.
 23. **Clarke R.** Currier S, Kaplan O, Gottesman M, Dickson RB. Effect of transfection with the MDR-1 cDNA on hormone responsiveness in MCF-7 cells. *J Natl Cancer Inst*, 84:1506-1512, 1992 (subject of Editorial).
 24. **Clarke R.** van den Berg HW & Murphy RF. Tamoxifen and 17 β -estradiol reduce the membrane fluidity of human breast cancer cells. *J Natl Cancer Inst*, 82:1702-1705, 1990.
 25. **Clarke R.** Brünner N, Katzenellenbogen BS, Thompson EW, Norman MJ, Koppi C, Paik S, Lippman ME & Dickson RB. Progression from hormone dependent to hormone independent growth in MCF-7 human breast cancer cells. *Proc Natl Acad Sci USA*, 86:3649-3653, 1989.
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Additional publications (Bioinformatics; selected)

1. Liu A, Zhang Y, Gehan E **& Clarke R.** Block principal components analysis with application to gene microarray data classification. *Stat Med*, 21: 3465-3474, 2002.
2. Wang Y, Lu J, Lee R **& Clarke R.** Iterative normalization of cDNA microarray data. *IEEE Trans Inf Technol Biomed*, 6: 29-37, 2002.
3. Wang Z, Wang Y, Xuan J, Dong Y, Bakay M, Khan J, **Clarke R.** & Hoffman, E.P. Optimized multilayer perceptrons for molecular classification and diagnosis using genomic data. *Bioinformatics*, 22: 755-761, 2006. 1
4. Wang J, Li H, Zhu Y, Yousef M, Mebozhyn M, Showe N, Xuan J, **Clarke, R.** & Wang, Y. VISDA: an open-source caBIG™ analytical tool for data clustering and beyond. *Bioinformatics*, 23: 2024-2027, 2007.
5. Zhang Y, Xuan J, de los Reyes BG, **Clarke R** & Resson HW. Identification of network motif-based transcription factor-target gene relationships by integrating multi-sources biological data. *BMC Bioinformatics*, 9:203, (18 pages as published on-line) 2008.
6. Chen L, Xuan J, Wang C, Shih L-M, Wang Y, Zhang Z, Hoffman EP, **& Clarke R.** Knowledge-guided multi-scale independent component analysis for biomarker identification. *BMC Bioinformatics*, 9: 416 (16 pages as published on-line), 2008.
7. **Clarke R.**, Resson H, Wang A, Xuan J, Liu, MC, Gehan E. & Wang Y. Properties of high dimensional data spaces: implications for exploring gene and protein expression data. *Nature Rev Cancer*, 8:37-49, 2008.
8. Wang, C., Xuan, J., Li, H., Wang, Y., Zhan, M., Hoffman, E.P. **& Clarke, R.** "Knowledge-guided gene ranking by coordinative component analysis." *BMC Bioinformatics*, 11:162, 2010 (13 pages as published on-line).
9. Zhang B, Li H, Riggins RB, Zhan M, Xuan J, Zhang Z, Hoffman EP, **Clarke R.** & Wang Y. Differential dependency network analysis to identify condition-specific topological changes in biological networks. *Bioinformatics*, 25: 526-532, 2009.
10. Chen L, Xuan J, Riggins RB, Wang Y, Hoffman EP **& Clarke R.** Multi-level support vector regression to identify condition-specific regulatory networks. *Bioinformatics*, in press, 2010.

RESEARCH SUPPORT - Robert Clarke Ph.D., D.Sc.

Ongoing Research Awards

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| NIH/NCI: U54-CA149147 | Clarke (PI) | 04/10-03/15 |
| <i>"Cancer Systems Biology: Integration of ER-related signaling in breast cancer."</i> This is a P01-style program grant with three projects, two cores, and two subcontracts (Virginia Tech; Fox Chase Cancer Center). The award is through the NCI Integrative Cancer Biology Program (ICBP) to establish a Center for Cancer Systems Biology. There are 11 such centers funded in the US through the current ICBP program. | | |
| NIH/NCI: R01-CA131465 | Clarke (PI) | 09/09-08/14 |
| <i>"Endocrine responsiveness in breast cancer."</i> This is a study of the interactions between RELA and XBP1 in the unfolded protein response and how they affect responsiveness to antiestrogens and aromatase inhibitors. | | |
| NIH/NCI: RFP No. S09-094 | Clarke (PI)/Madhavan (Co-PI) | 08/09-07/12 |
| <i>"caBIG In Silico Research Centers of Excellence."</i> This award funds a Center of Excellence to provide innovative bioinformatics and high dimensional data analysis, research support, and tool development within the caBIG community. Dr. Clarke is the Scientific Director and Dr. Madhavan is Project Director (co-PIs). | | |
| Department of Defense: BC073977 | Clarke (PI) | 05/08-04/11 |
| <i>"XBP1 and Endocrine Responsiveness."</i> This is a DOD BCRP Idea award to study the role of XBP1 in affecting breast cancer cell growth. | | |
| NIH/NCI: R21 CA139246-01 | Xuan (PI)/Clarke (subcontract PI) | 06/09-05/11 |
| <i>"Network-based Prediction of Antiestrogen Resistance in Breast Cancer."</i> This application is to develop <i>in silico</i> methods for predicting signaling associated with antiestrogen resistance <i>in vitro</i> . Dr. Xuan is PI (Virginia Tech) - Dr. Clarke is PI on a subcontract to assist in data interpretation and to perform wet-lab validations studies on candidate genes. | | |
| Komen Foundation: KG090245 | Clarke (PI) | 08/09-07/12 |
| <i>"IRF1 in Breast Cancer."</i> This is a study of the role of IRF1 as a regulator of antiestrogen resistance in breast cancer cells. | | |
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NIH/NCI: 1P30-CA51008 **Weiner (PI)** 09/90-08/10

“Lombardi Comprehensive Cancer Center Support Grant – Breast Cancer Program.” This application funds a research program within the Lombardi Comprehensive Cancer Center. Dr. Weiner is PI of the CCSG and Cancer Center Director - Dr. Clarke is the basic science Co-Director of the Breast Cancer Program; Dr. Claudine Isaacs is the clinical Co-Director of the Breast Cancer Program.

NIH/NCI: R01CA096846 **Bouton (PI)/Clarke (subcontract PI)** 05/09-04/13

“Mechanisms of Breast Tumor Cell Growth, Motility, and Antiestrogen Response.” This proposal seeks to understand the action of a signaling axis that may function as a mediator of these aggressive breast tumor phenotypes, focusing on the protein tyrosine kinase c-Src, the adapter molecule p130Cas (Cas), and a cytoplasmic molecule called breast cancer antiestrogen resistance-3 (BCAR3).

Recently Completed Awards

NIH/NCI: U54-CA100970 **Hilakivi-Clarke (PI)/Clarke (Co-PI)** 08/03-12/09

“Timing of Dietary Exposure and Breast Cancer Risk.” This was a P01-style program award with four projects and two cores that studied different lifetime dietary exposures in humans and experimental models. Collaborating sites with subcontracts included the University of Illinois at Champagne-Urbana (Dr. W. Helferich), two Finnish universities (Univ. Tampere; Dr. R. Luotto and Univ. Turku; Dr. S. Makela), and Virginia Tech (Dr. Y. Wang).

NIH/NCI: R01-CA096483 **Clarke (PI)** 09/03-08/09

“Bioengineering Research Group: Molecular Analysis of Breast Cancer.” This was a Bioengineering Research Group award to identify prospectively molecular profiles and design neural network and biostatistical model based classifiers that predict recurrence, independent of treatment, in early stage breast cancers. Collaborating sites with subcontracts included the University of Edinburgh, Scotland (Dr. W.R. Miller) and Virginia Tech (Dr. Y. Wang).
