

## BIOGRAPHICAL SKETCH

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NAME Saraswati Sukumar		POSITION TITLE	
eRA COMMONS USER NAME SSUKUMA1		Professor of Oncology/Pathology	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Nagpur University, Nagpur, India	M.S.	1969	Biochemistry
Atomic Energy Commission at Cancer Institute, Madras, India	Research Fellow	1971-76	Microbiology
Nagpur University, Nagpur, India	Ph.D.	1977	Biochemistry
National Cancer Institute, NIH, Bethesda, MD	Postdoc Fellow	1978-83	Immunology, Molecular Biology

### A. Positions and Honors

#### Positions and Employment

- 1978-1983 Visiting Associate, Laboratory of Immunobiology, National Cancer Institute, Bethesda, MD
- 1983-1988 Scientist Associate, NCI and Bionetics Research Inc., NCI/Frederick Cancer Research Facility, Frederick, MD (Section Chief, Mariano Barbacid)
- 1989-1994 Assistant Professor, Molecular Biology of Breast Cancer Laboratory, The Salk Institute for Biological Studies, La Jolla, CA
- 1994-2001 Associate Professor of Oncology and
- 1996-2001 Associate Professor of Pathology, JHUSOM, Baltimore, MD
- 1996-2001 Associate Professor in Human Genetics, JHUSOM, Baltimore, MD
- 2000-2002 Associate Professor of Pathobiology, JHUSOM, Baltimore, MD
- 2002-present Barbara B. Rubenstein Professor of Oncology and Pathology, Director of Basic Research; Breast Cancer Program, The Johns Hopkins University School of Medicine, Baltimore, MD
- 2002-2004 Soo Lin Professor and Head of Breast Cancer Laboratories, ORI, National University of Singapore
- 2002-present Professor in Human Genetics, JHUSOM, Baltimore, MD
- 2002-present Preceptor in Graduate Programs in- Pathobiology, Center for Molecular Medicine, JHUSOM, Baltimore, MD
- 2004-present Professor of Pathology, JHUSOM, Baltimore, MD

#### Other Experience and Professional Memberships

- 1994-2005 Director of Basic Research, Breast Cancer Program, SKCCC at Johns Hopkins, Baltimore, MD
- 2005-present Co-Director, Breast Cancer Program at Johns Hopkins, SKCCC, Baltimore, MD
- 2007-present Member of the Scientific Advisory Board, Susan G. Komen Foundation for the Cure

### B. Selected peer-reviewed publications (in chronological order).

(Selected from 130 peer-reviewed publications)

- Chen H, Chung S and Sukumar S. Hoxa5-induced apoptosis in breast cancer cells is mediated by caspases 2 and 8. *Molecular Cellular Biology* 24: 924-935, 2004.
- Mehrotra J, Ganpat MM, Kanaan Y, Fackler MJ, McVeigh M, Lahti-Domenici J, Polyak, K, Argani P, Naab, T, Garrett E, Parmigiani G, Broome C and Sukumar S. ER/PR-negative breast cancers of young African American women have a higher frequency of methylation of multiple genes than those of Caucasian women. *Clin Cancer Res* 10:2052-2057, 2004.
- Kominsky SL, Vali M, Korz M, Gabig TG, Garrett E, Argani P, and Sukumar S. Clostridium perfringens enterotoxin elicits rapid and specific cytolysis of breast carcinoma cells mediated through tight junction proteins Claudin 3 and 4. *Amer J Pathol* 164:1627-1633, 2004.

Program Director/Principal Investigator (Last, First, Middle): Bhujwala, Zaver, M.

- Mehrotra J, Vali M, McVeigh M, Kominsky SL, Fackler MJ, Lahti-Domenici J, Polyak K, Sacchi N, Argani P, and Sukumar S. Very high frequency of hypermethylated genes in breast cancer metastasis to the bone, brain, and lung. *Clin Cancer Res* 10: 3104-3109, 2004.
- Fackler MJ, McVeigh M, Mehrotra J, Blum MA, Lange J, Lapidus A, Garrett E, Argani P, and Sukumar S. Quantitative multiplex methylation specific PCR assay for the detection of promoter hypermethylation in multiple genes in breast cancer. *Cancer Res* 64:4442-4452, 2004.
- Bae YK, Brown A, Garrett E, Bornman D, Fackler MJ, Sukumar S, Herman JG, Gabrielson E. Hypermethylation in histologically distinct classes of breast cancer *Clin Cancer Res* 10:5998-6005, 2004.
- Parker BS, Argani P, Cook BP, Liangfeng H, Chartrand SD, Zhang M, Saha S, Bardelli A, Jiang Y, St Martin TB, Nacht M, Teicher BA, Klinger KW, Sukumar S, Madden SL. Alterations in vascular gene expression in invasive breast carcinoma. *Cancer Res* 64(21):7857-66, 2004.
- Chen H, Rubin E, Zhang H, Chung S, Jie CC, Garrett E, Biswal S, Sukumar S. Identification of transcriptional targets of HOXA5. *J Biol Chem* 280(19):19373-80, 2005.
- Li J, Zhao J, Yu X, Lane JR, Kuerer H, Krishnamurthy S, Schilling E, Khan SA, Sukumar S, Chan DW. Identification of biomarkers for breast cancer in nipple aspiration and ductal lavage fluid. *Clin Cancer Res*. 11(23):8312-20, 2005.
- Wu G, Xing M, Mambo E, Huang X, Liu J, Guo Z, Chatterjee A, Goldenberg D, Gollin SM, Sukumar S, Trink B, and Sidransky D. Somatic mutation and gain of copy number of PIK3CA in human breast cancer, *Breast Cancer Res*. 7: R609-16, 2005.
- Davidson NE and Sukumar S. Of Snail, mice, and women, *Cancer Cell*. 8: 173-4, 2005.
- Lo PK, Mehrotra J, D'Costa A, Fackler MJ, Garrett-Mayer E, Argani P, Sukumar S. Epigenetic Suppression of secreted frizzled related protein 1 (SFRP1) expression in human breast cancer. *Cancer Biol Ther*. 5(3), [Epub ahead of print] 2006.
- Murata S, Kominsky SL, Vali M, Zhang Z, Garrett-Mayer E, Korz D, Huso D, Baker SD, Barber J, Jaffee E, Reilly RT, Sukumar S. Ductal access for prevention and therapy of mammary tumors. *Cancer Res*. 66(2):638-45, 2006.
- Swift-Scanlan T, Blackford A, Argani P, Sukumar S, Fackler MJ. Two-color quantitative multiplex methylation-specific PCR. *Biotechniques*. 40(2):210-9, 2006.
- Liang X, Lau QC, Salto-Tellez M, Putti TC, Loh M, and Sukumar S. Mutational hotspot in Exon 20 of PIK3CA in Breast Cancer among Singapore Chinese. *Cancer Bio and Ther*. 2006 May 6; 5 (5)
- Fackler MJ, Malone K, Zhang Z, Schilling E, Garrett-Mayer E, Swift-Scanlan T, Lange J, Nayar R, Davidson NE, Khan SA, Sukumar S. Quantitative multiplex methylation-specific PCR analysis doubles detection of tumor cells in breast ductal fluid. *Clin Cancer Res*. 12: 3306-3310, 2006.
- Lau QC, Raja E, Salto-Tellez E, Liu Q, Ito K, Inoue M, Putti TC, Loh M, Ko TK, Huang C, Ito Y, and Sukumar S, RUNX3 is frequently inactivated by dual mechanisms in breast carcinoma: Protein mislocalization and promoter hypermethylation *Cancer Res*. 66:6512-6520, 2006.
- Wu X, Chen H, Parker B, Rubin E, Zhu T, Lee JS, Argani P, Sukumar S. HOXB7, a homeodomain protein, is overexpressed in breast cancer and confers epithelial-mesenchymal transition. *Cancer Res*. 2006 Oct 1;66(19):9527-34
- Visvanathan K, Sukumar S, Davidson NE Epigenetic biomarkers and breast cancer: cause for optimism. *Clin Cancer Res*. 2006 Nov 15;12(22):6591-3.
- Rubin E, Wu X, Zhu T, Cheung JC, Chen H, Lorincz A, Pandita RK, Sharma GG, Ha HC, Gasson J, Hanakahi LA, Pandita TK, Sukumar S. A role for the HOXB7 homeodomain protein in DNA replication. *Cancer Res*. 2007 Feb 15;67(4):1527-35.
- Shipitsin M, Campbell LL, Argani P, Weremowicz S, Bloushtain-Qimron N, Yao J, Nikolskaya T, Serebryiskaya T, Beroukhim R, Hu M, Halushka MK, Sukumar S, Parker LM, Anderson KS, Harris LN, Garber JE, Richardson AL, Schnitt SJ, Nikolsky Y, Gelman RS, Polyak K. Molecular definition of breast tumor heterogeneity. *Cancer Cell*. 2007 Mar;11(3):259-73
- Chen H, Zhang H, Lee J, Liang X, Wu X, Zhu T, Lo PK, Zhang X, Sukumar S. HOXA5 acts directly downstream of retinoic acid receptor  $\beta$  and contributes to retinoic acid induced apoptosis and growth inhibition. *Cancer Res*. 2007 Sep 1;67(17):8007-13.
- Kominsky SL, Tyler B, Sosnowski J, Brady K, Doucet M, Nell D, Smedley JG 3rd, McClane B, Brem H, Sukumar S. Clostridium perfringens Enterotoxin as a Novel-Targeted Therapeutic for Brain Metastasis. *Cancer Res*. 2007 Sep 1;67(17):7977-82.
- Han L, Witmer PD, Casey E, Valle D, Sukumar S. DNA Methylation Regulates MicroRNA Expression.

Program Director/Principal Investigator (Last, First, Middle): Bhujwalla, Zaver, M.

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Wood LD, Parsons DW, Jones S, Lin J, Sjoblom T, Leary RJ, Shen D, Boca SM, Barber T, Ptak J, Silliman N, Szabo S, Dezso Z, Ustyansky V, Nikolskaya T, Nikolsky Y, Karchin R, Wilson PA, Kaminker JS, Zhang Z, Croshaw R, Willis J, Dawson D, Shipitsin M, Willson JK, Sukumar S, Polyak K, Park BH, Pethiyagoda CL, Pant PV, Ballinger DG, Sparks AB, Hartigan J, Smith DR, Suh E, Papadopoulos N, Buckhaults P, Markowitz SD, Parmigiani G, Kinzler KW, Velculescu VE, Vogelstein B. The Genomic Landscapes of Human Breast and Colorectal Cancers. *Science*. 2007, 1108-13.

Gupta A, Guerin-Peyrou TG, Sharma GG, Park C, Agarwal M, Ganju RK, Pandita S, Choi K, Sukumar S, Pandita RK, Ludwig T, Pandita TK. Mammalian Ortholog of Drosophila MOF that Acetylates Histone H4 Lysine16 is Essential for Embryogenesis and Oncogenesis. *Mol Cell Biol*. 2008 Jan;28(1):397-409

Wu JM, Fackler MJ, Halushka MK, Molavi DW, Taylor ME, Teo WW, Griffin C, Fetting J, Davidson NE, De Marzo AM, Hicks JL, Chitale D, Ladanyi M, Sukumar S, Argani P. Heterogeneity of breast cancer metastases: comparison of therapeutic target expression and promoter methylation between primary tumors and their multifocal metastases. *Clin Cancer Res*. 2008 Apr 1;14(7):1938-46

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Lee JS, Fackler MJ, Teo WW, Lee JH, Choi C, Park MH, Yoon JH, Zhang Z, Argani P, Sukumar S. Quantitative promoter hypermethylation profiles of ductal carcinoma in situ in North American and Korean women: Potential applications for diagnosis. *Cancer Biol Ther*. 2008 Sep;7(9):1398-406.

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Marlow R, Strickland P, Lee JS, Wu X, Pebenito M, Binnewies M, Le EK, Moran A, Macias H, Cardiff RD, Sukumar S, Hinck L. SLITs suppress tumor growth in vivo by silencing Sdf1/Cxcr4 within breast epithelium. *Cancer Res*. 2008 Oct 1;68(19):7819-27.

Lo PK, Sukumar S. Epigenomics and breast cancer. *Pharmacogenomics*. 2008 Dec;9(12):1879-902.

Cao D, Polyak K, Halushka MK, Nassar H, Kouprina N, Iacobuzio-Donahue C, Wu X, Sukumar S, Hicks J, De Marzo A, Argani P. Serial analysis of gene expression of lobular carcinoma in situ identifies down regulation of claudin 4 and overexpression of matrix metalloproteinase 9. *Breast Cancer Res*. 2008 Oct 27;10(5):R91.

Mankoo PK, Sukumar S, Karchin R. PIK3CA somatic mutations in breast cancer: Mechanistic insights from Langevin dynamics simulations. *Mankoo PK, Sukumar S, Karchin R. Proteins*. 2008 Sep 10.

Fackler MJ, Rivers A, Teo WW, Mangat A, Taylor E, Zhang Z, Goodman S, Argani P, Nayar R, Susnik B, Sukumar S, Khan SA. Hypermethylated Genes as Biomarkers of Cancer in Women with Pathologic Nipple Discharge. *Clin Cancer Res*. 2009 May 26. [Epub ahead of print]

Lo PK, Watanabe H, Cheng PC, Teo WW, Liang X, Argani P, Lee JS, Sukumar S. MethSYBR, a novel quantitative PCR assay for the dual analysis of DNA methylation and CpG methylation density. *J Mol Diagn*. 2009 Sep;11(5):400-14.

### **C. Research Support.**

#### **Ongoing Research Support**

P50 CA88843-07 (Sukumar) 09/30/00-08/29/11

NIH/NCI

Specialized Program in Research Excellence (SPORE in Breast Cancer)

This grant consists of four projects and two cores.

P50 CA88843-07 (Sukumar) 09/30/00-08/29/11

NIH/NCI

Specialized Program in Research Excellence (SPORE in Breast Cancer)

Project 1: Molecular Markers for Breast Cancer

The overall goal of this proposal is to identify major molecular alterations in carcinoma of the breast by microarray analysis of all stages of tumor development, and develop markers for early detection.

BC030054 Center of Excellence in Breast Cancer (Sukumar) 08/30/04-12/31/09

Program Director/Principal Investigator (Last, First, Middle): Bhujwalla, Zaver, M.

Department of Defense

Prevention and Therapy of Metastatic Breast Cancer

This is a multi-institutional team of 5 researchers, and three resource directors who will jointly study metastatic breast cancer. Dr. Sukumar will perform SAGE and validate, and investigate promising candidate gene markers, develop cell line and xenografts models for imaging, developing drugs, and immunotherapy by the other members of the COE.

AVON Foundation (Sukumar)

06/30/09-05/31/10

This grant supports critical infrastructure of the Johns Hopkins AVON Breast Center, patient support and advocacy, career development and research in the breast cancer program.

Avon Foundation (Sukumar and Polyak)

11/1/06-10/31/09

Understanding the molecular basis of parity-induced protection against breast cancer through global expression and epigenetic profiles

Role: Co-Principal Investigator

Avon Foundation (Stearns, Sukumar and Khan)

06/1/09-06/01/11

Gene methylation and estradiol levels in random FNA samples as biomarkers for breast cancer risk

The goal of this proposal is to develop molecular markers that will predict risk better than the Gail model.

Role: Co-Principal Investigator

Susan G. Komen Foundation for the Cure (Karchin and Sukumar)

07/1/08-06/31/11

Integrating computational and experimental biology to discover novel biomarkers: activating mutations in the breast cancer oncogene PIK3CA

Role: Co-Principal Investigator

Windy Hill (Sukumar)

05/01/06-12/31/09

The effectiveness of 5 fluorouracil and other chemotherapies given intraductally to prevent and treat mammary tumors in rats.

DOD Era of Hope Scholar Pandey (Sukumar)

12/01/05-11/30/10

Department of Defense

Proteomic and functional analysis of fibroblasts in breast cancer.

Role: Co-Investigator

**Completed Research Support**

From 1989 onwards, more than 20 grants from NIH, DOD, Susan G Komen Foundation, AVON Foundation, Entertainment Industry Foundation and other granting agencies.